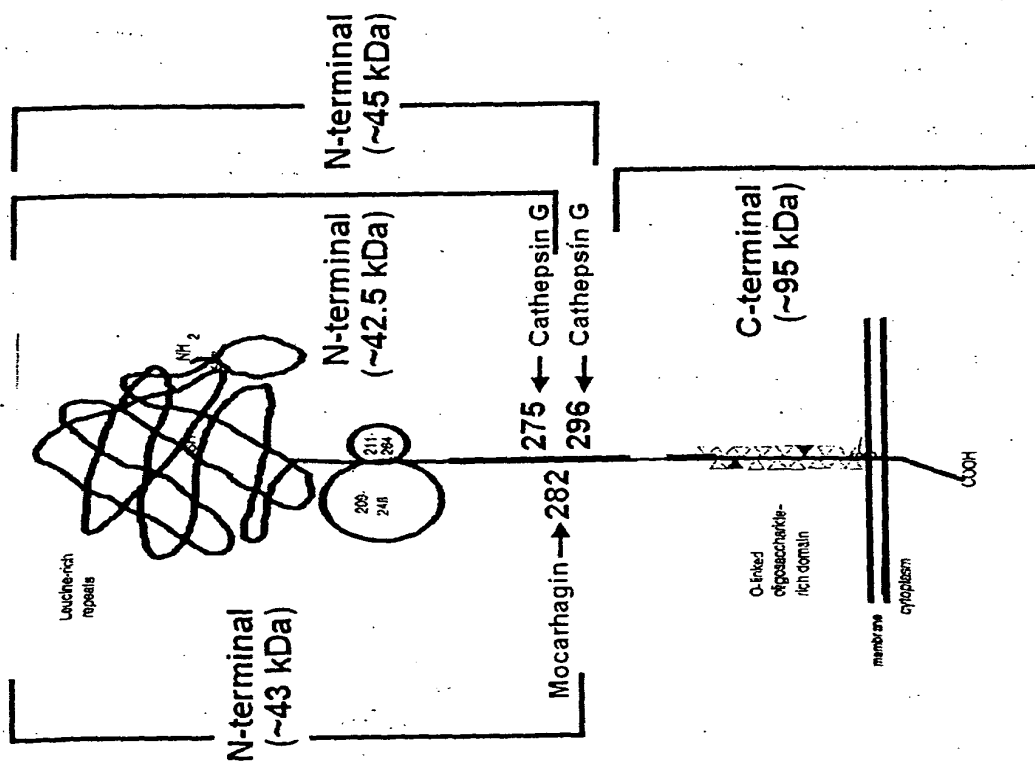


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FIG. 1

Cleavage sites of endoproteases on the α -chain of GPIb

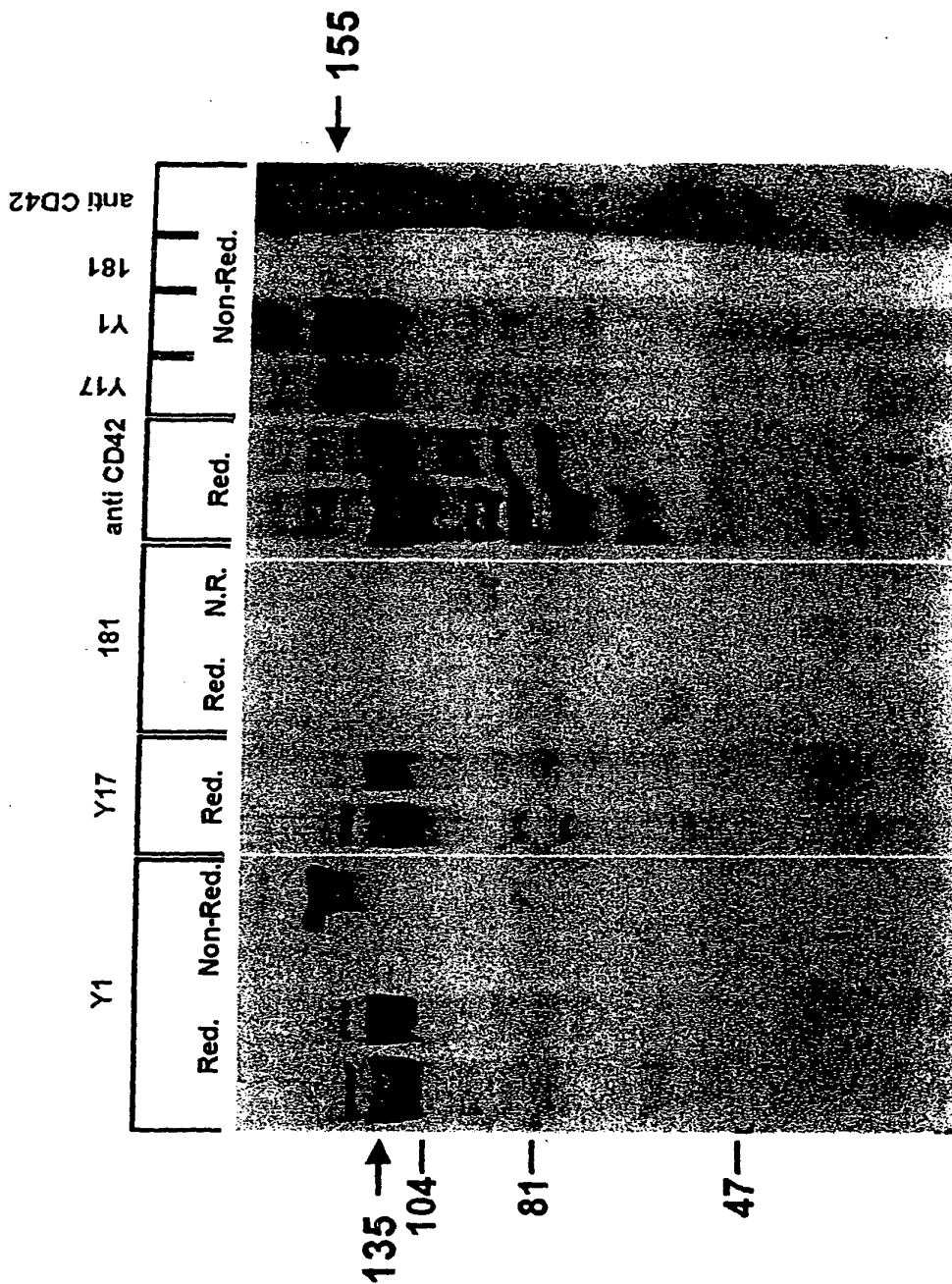


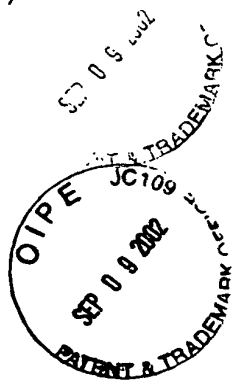


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FIG. 2

Binding of Y1 and Y17 to platelets in reduced and non-reduced conditions





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Characterization of Optimal Determinants for Binding of Y1 to It's Ligands

FIG. 3

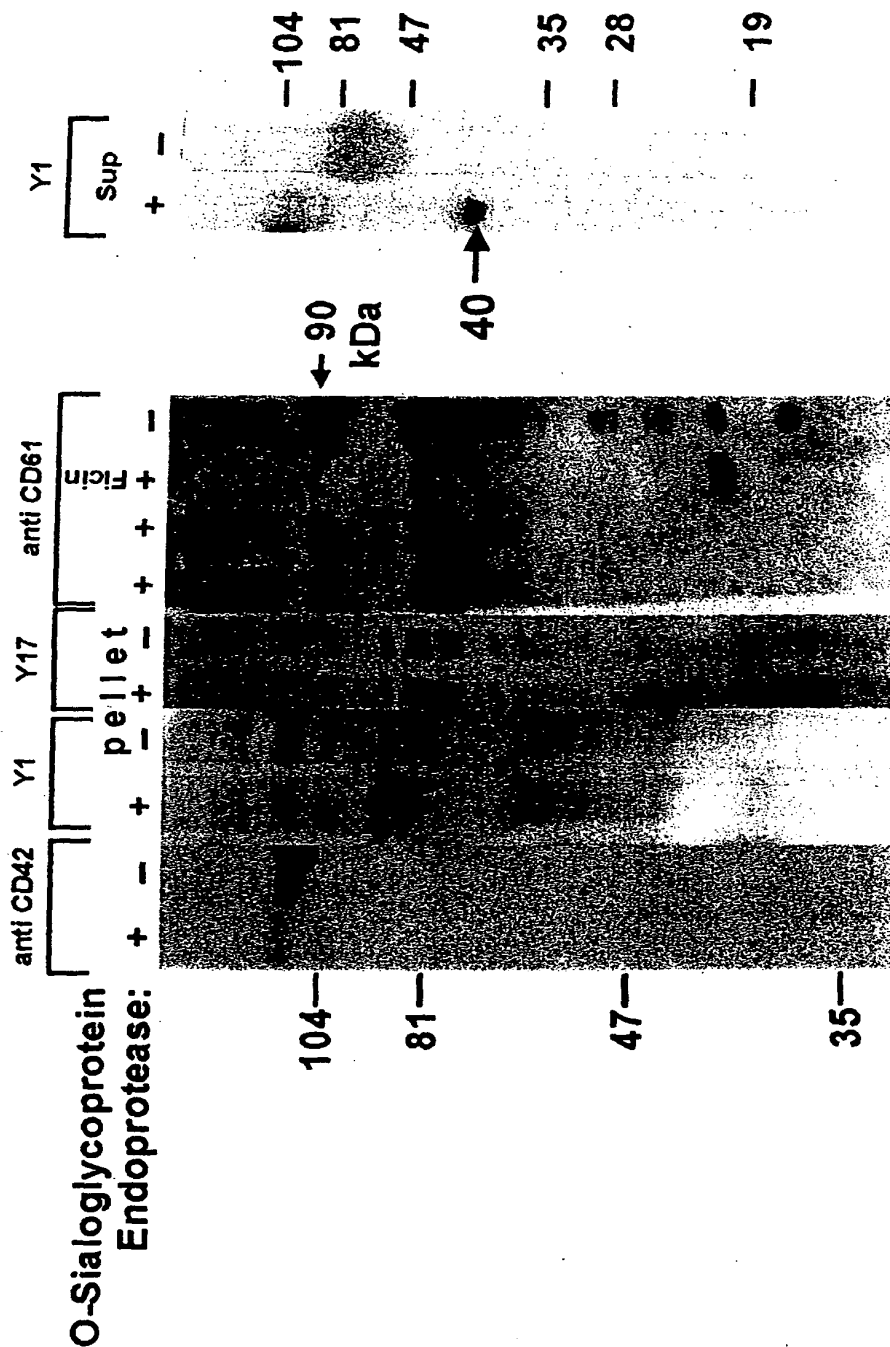
	Platelets/GC	KG1/RP-HPLC #4
Rec: GP1b 1-340 GP1b 1-480	- -	
Glycanase: N N+O	+ +	+++ +++
Proteases: Mocarhagin O-Sialo Peptidase Ficin Trypsine Elastase	++ (~40kD) ++ (~40kD) - ++ (~40kD) ++ (~40kD)	- - - - ++
Sulfatase (Aryl)		-/+



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FIG. 4

Cleavage of platelets GPIb by O-Sialoglycoprotein abolishes binding of both Y1 and Y17

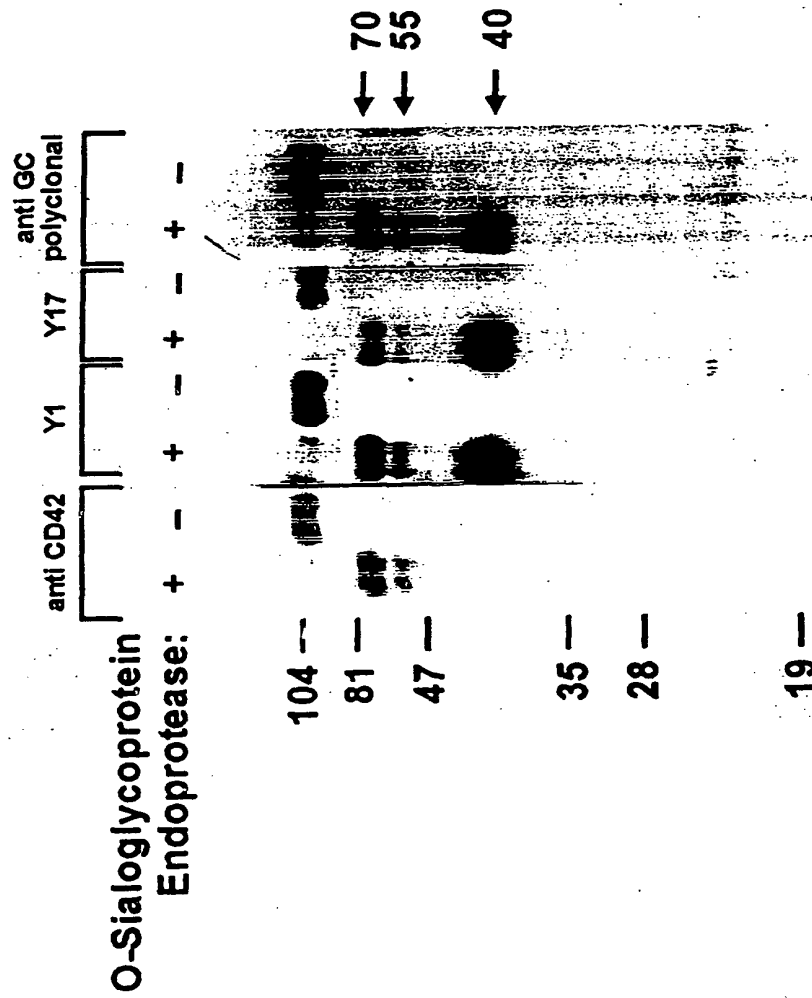




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FIG. 5

Y1 and Y17 binds similar glyocalycin fragments after cleavage by O-Sialoglycoprotein Endoprotease

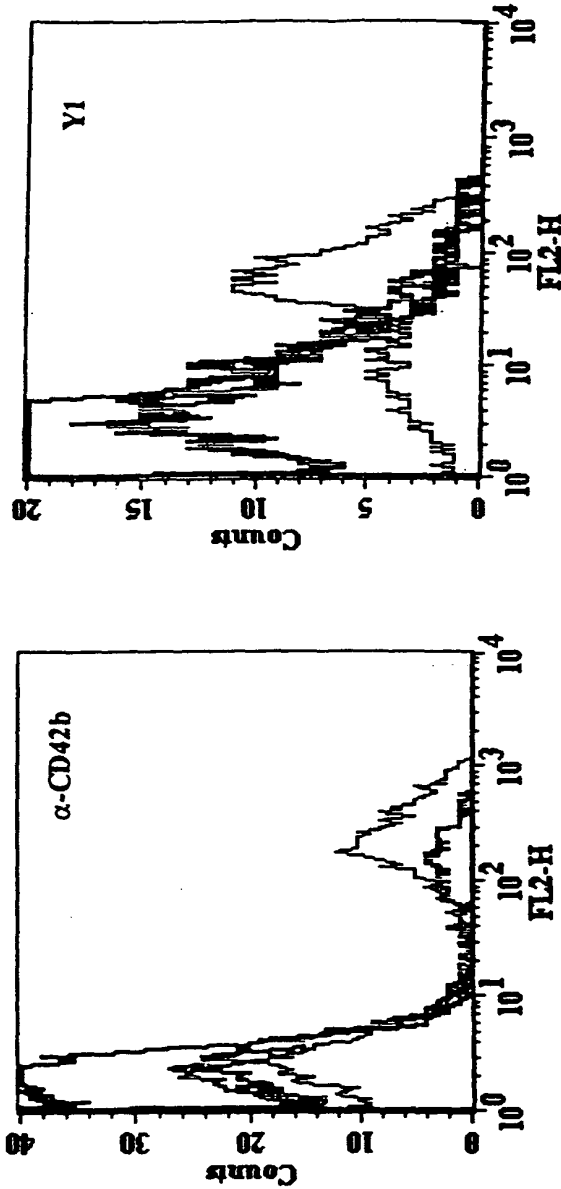




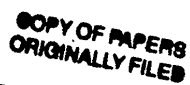
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Specific GPIIb Proteolysis Abolishes Y1 Binding to Platelets

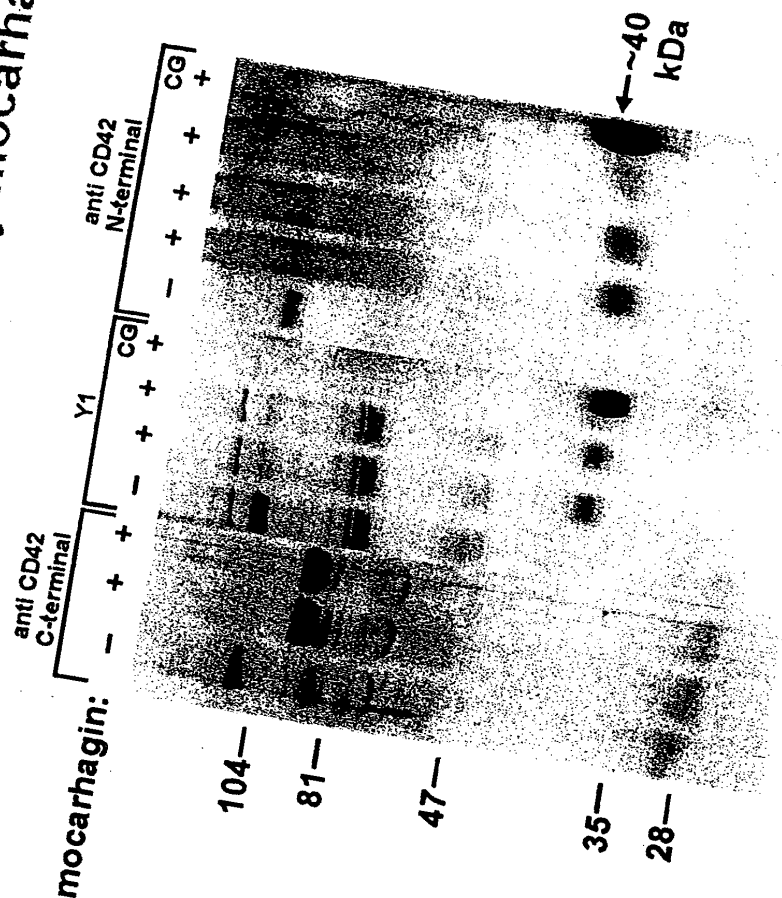
FIG. 6



Key	Name	Parameter	G
	NON-TREATED PLATELETS		
—	O-SIALOGLYCOPROTEIN ENDO. (10 μg/ml)		
—	O-SIALOGLYCOPROTEIN ENDO. (50 μg/ml)		
—	FICIN (18 μg/ml)		



Y1 binds N-terminal (His-1 - Glu 282) fragment of platelet GPIIb after cleavage by mocarhagin

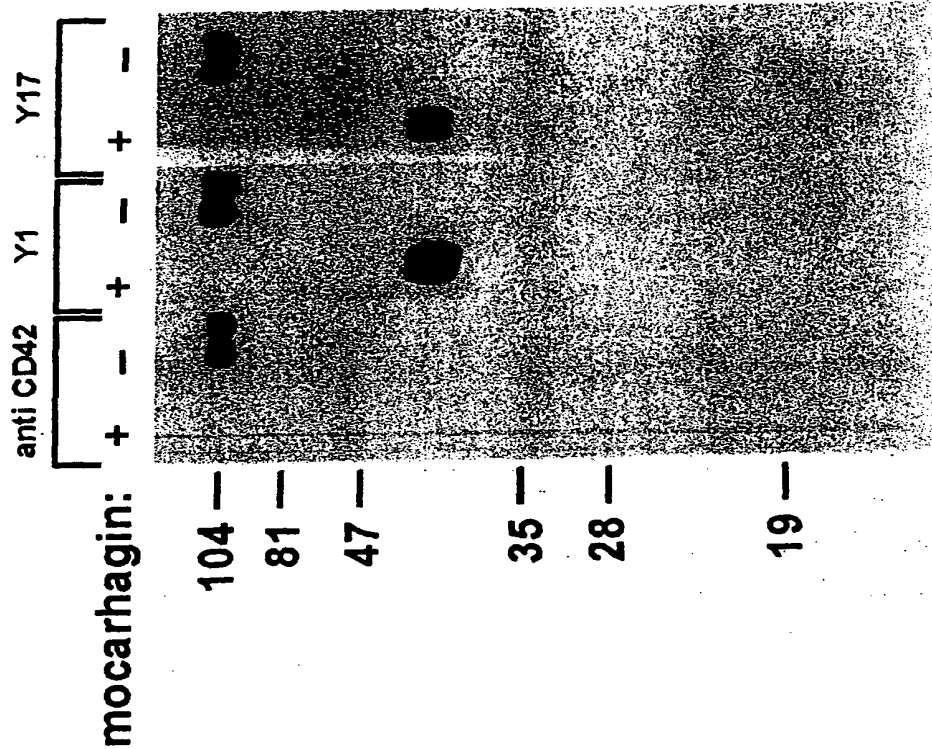




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FIG. 8

Binding of Y1 and Y17 to glycolalycin after
cleavage by mocarhagin

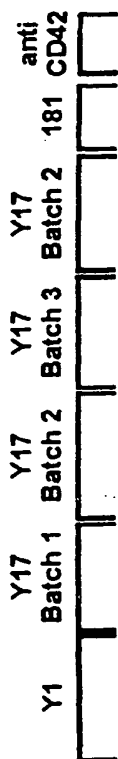




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FIG. 9

Binding of Y1 and Y17 to platelets



104—

81—

47—

35—

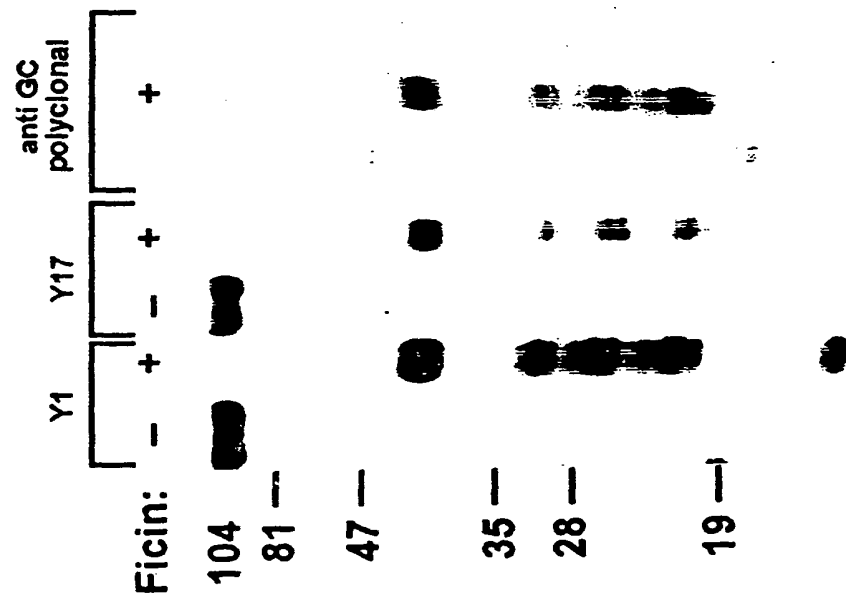
28—



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FIG. 10

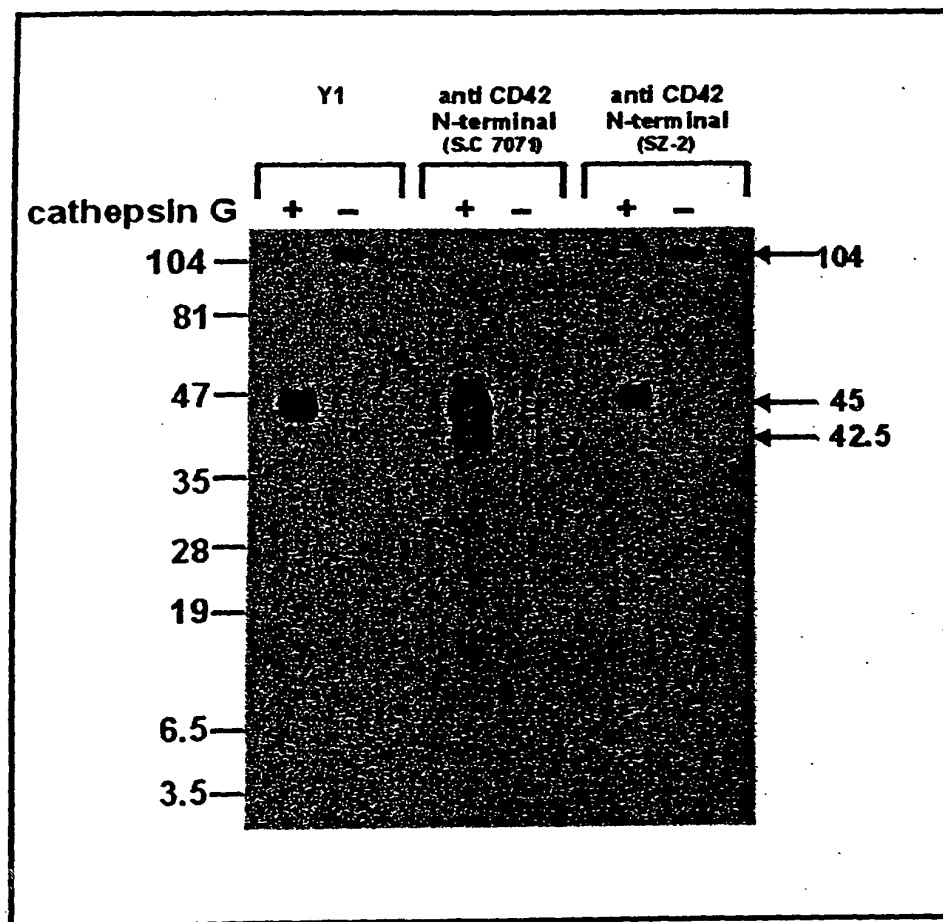
Y1 and Y17 bind glycoprotein similar after cleavage by Ficin





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FIG. 11

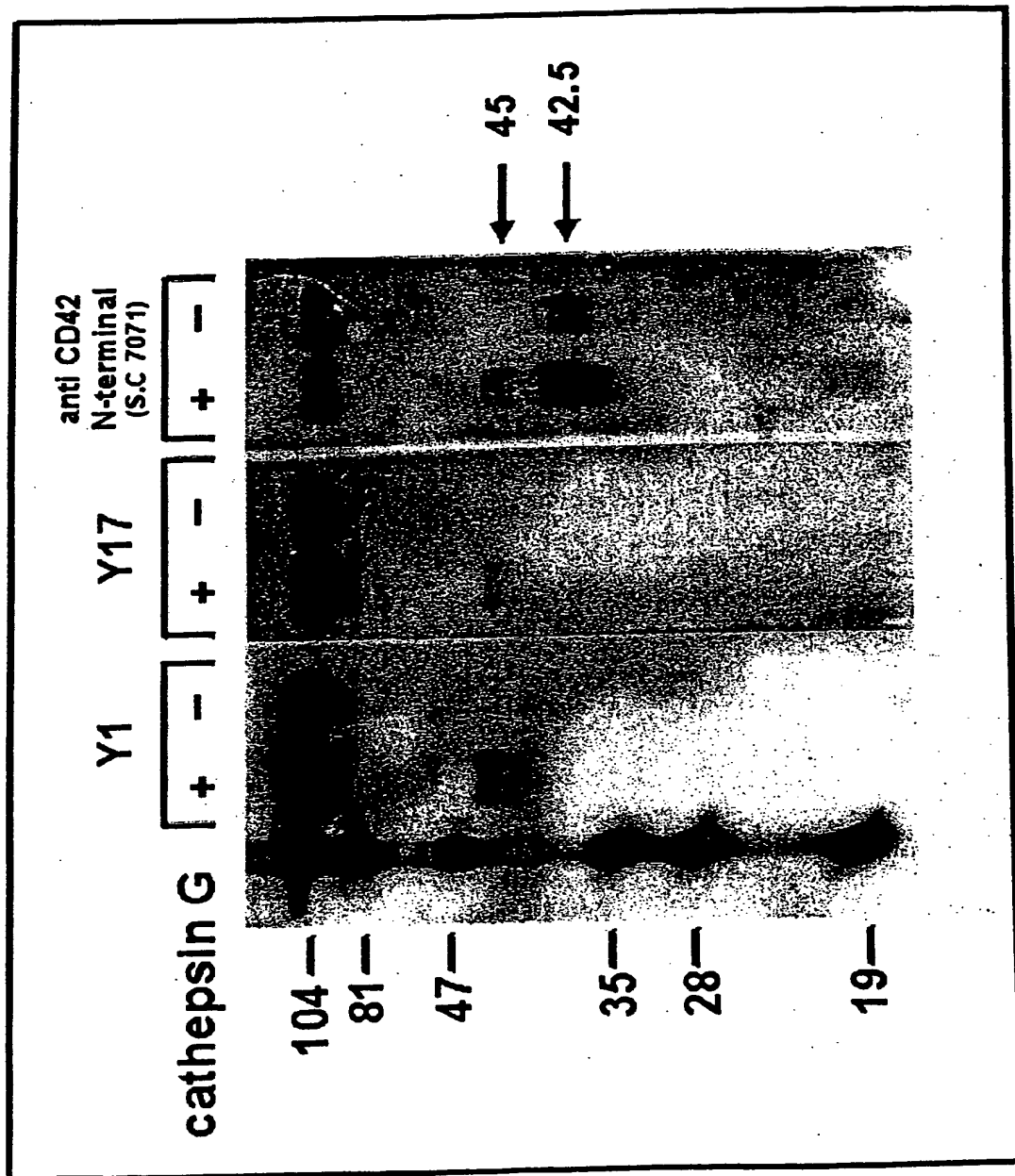




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FIG. 12

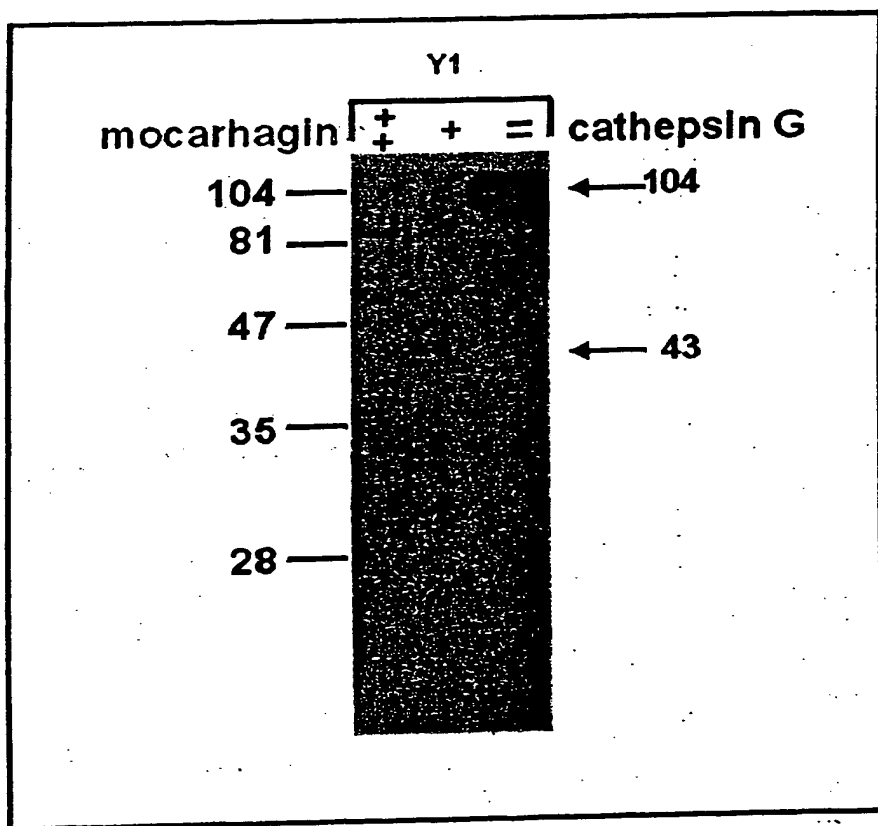
Y1 and Y17 reacts with larger cathepsin G cleaved
platelets GPIIb fragment





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FIG. 13

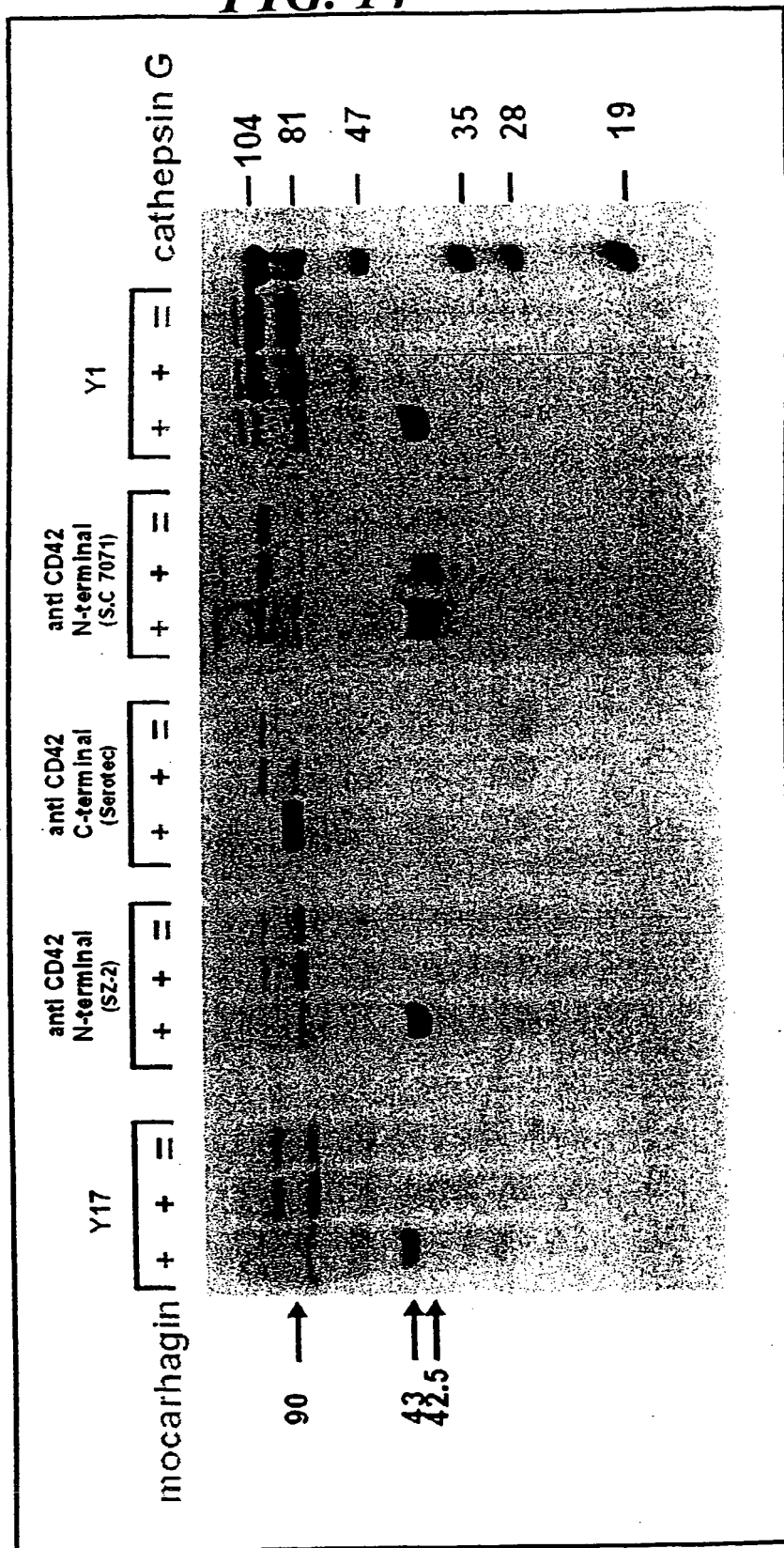


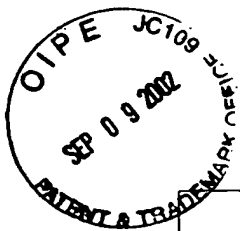


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Cleavage of washed platelets by mocarhagin and cathepsin G

FIG. 14

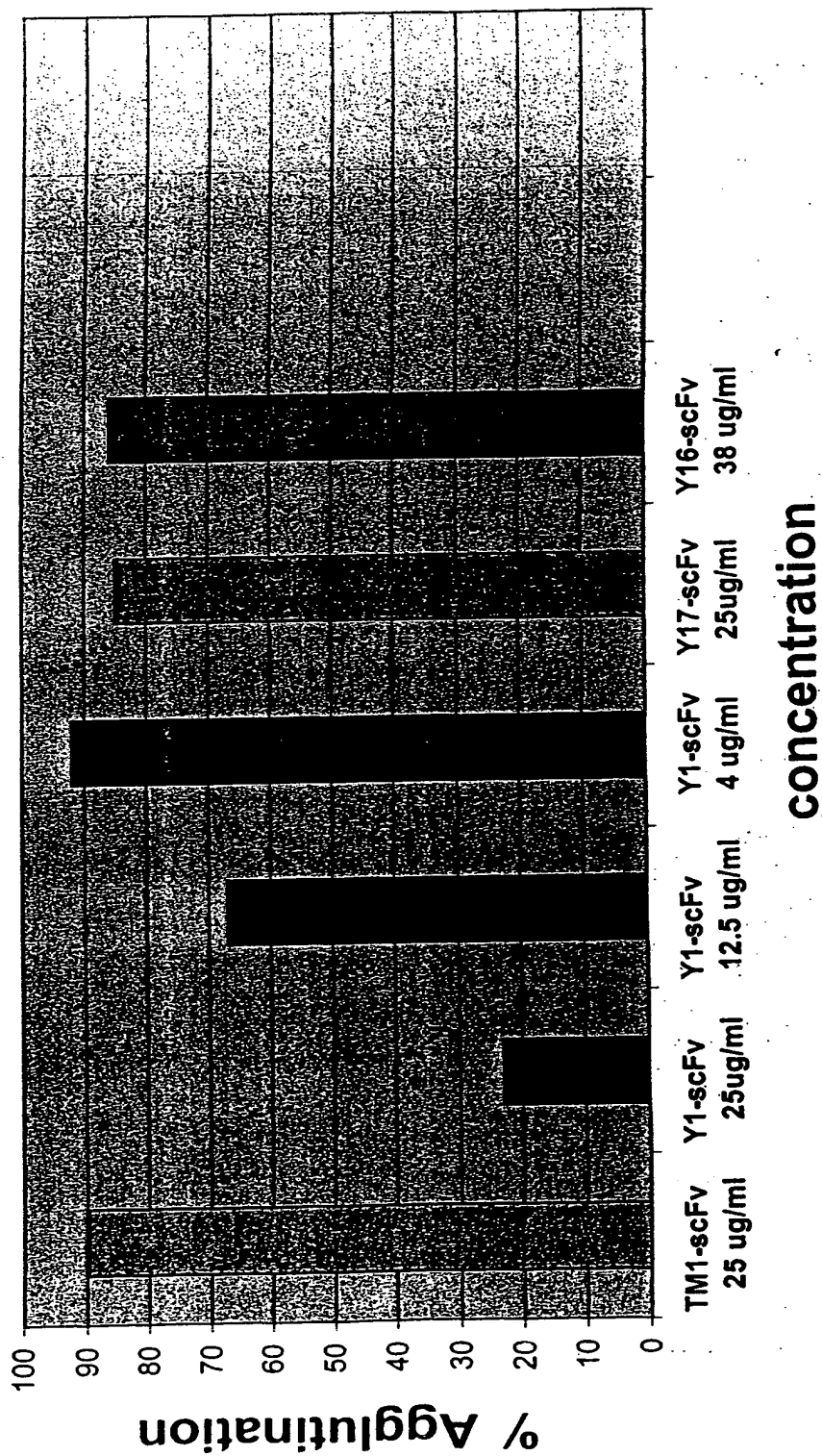


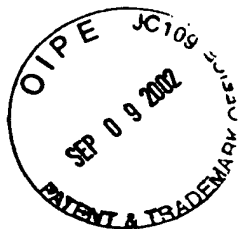


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FIG. 15

Influence of Y1-scFv on platelets agglutination in washed platelets





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FIG. 16

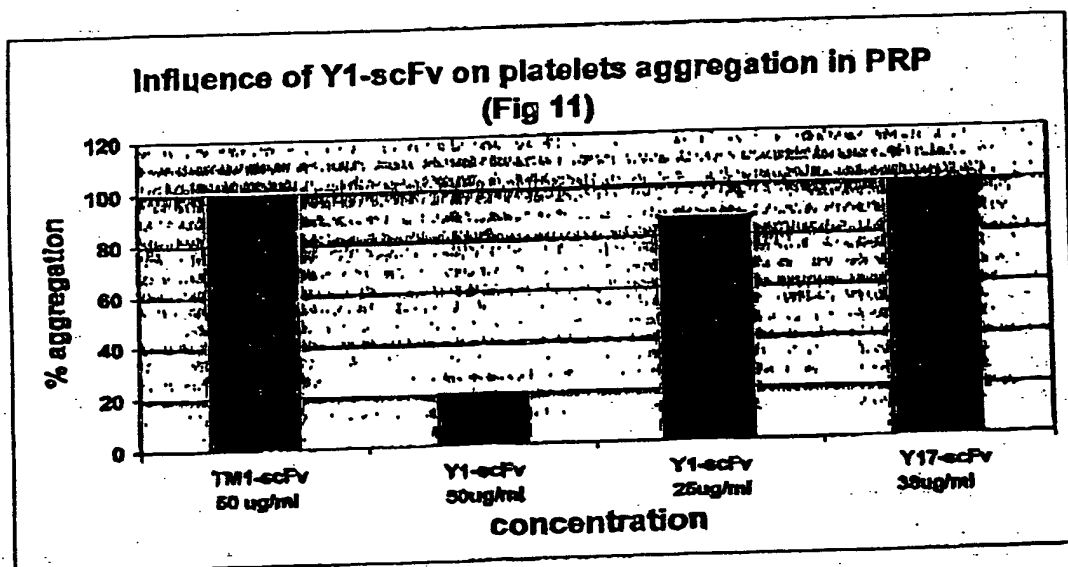
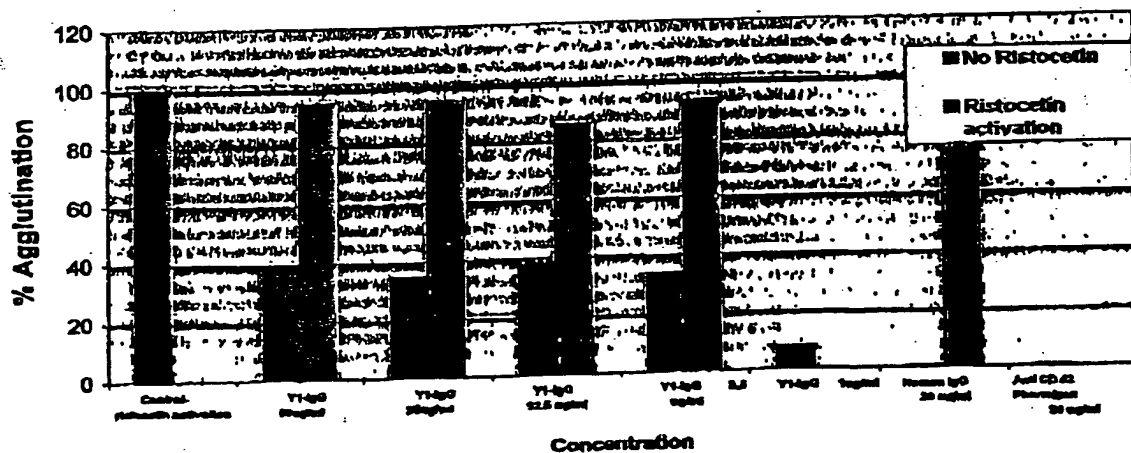




FIG. 17

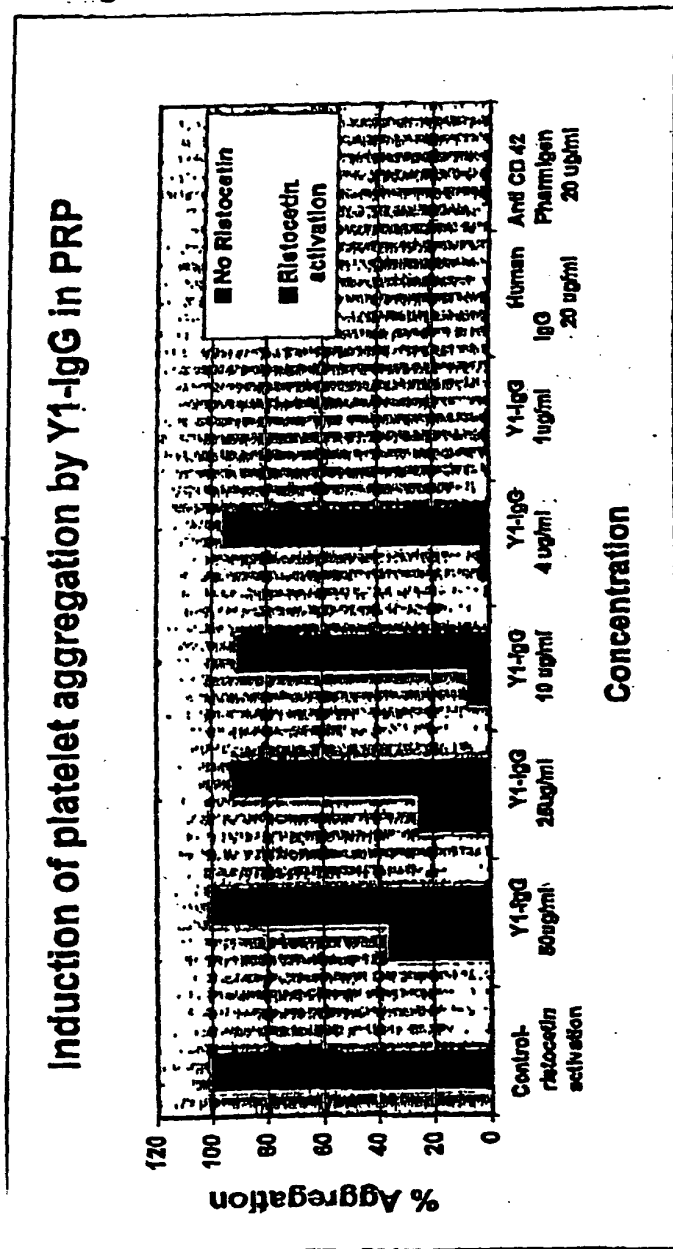
Induction of platelet agglutination by Y1-IgG in washed platelets





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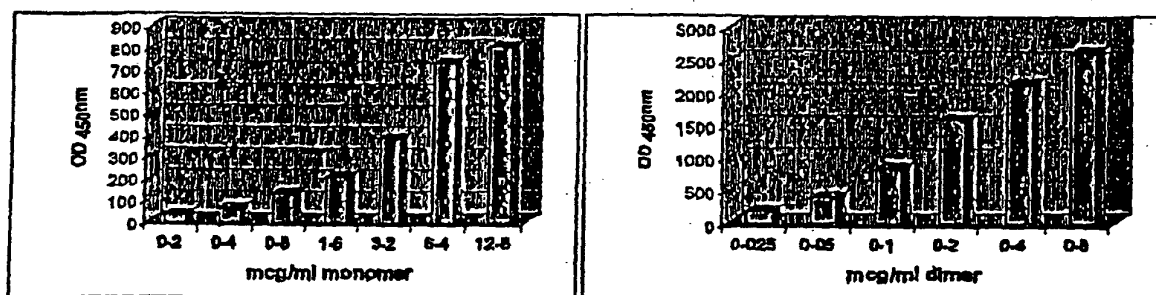
FIG. 18





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FIG. 19





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Specificity of Binding of Y1 and α -CD42 (N1-19) to their Ligands

FIG. 20

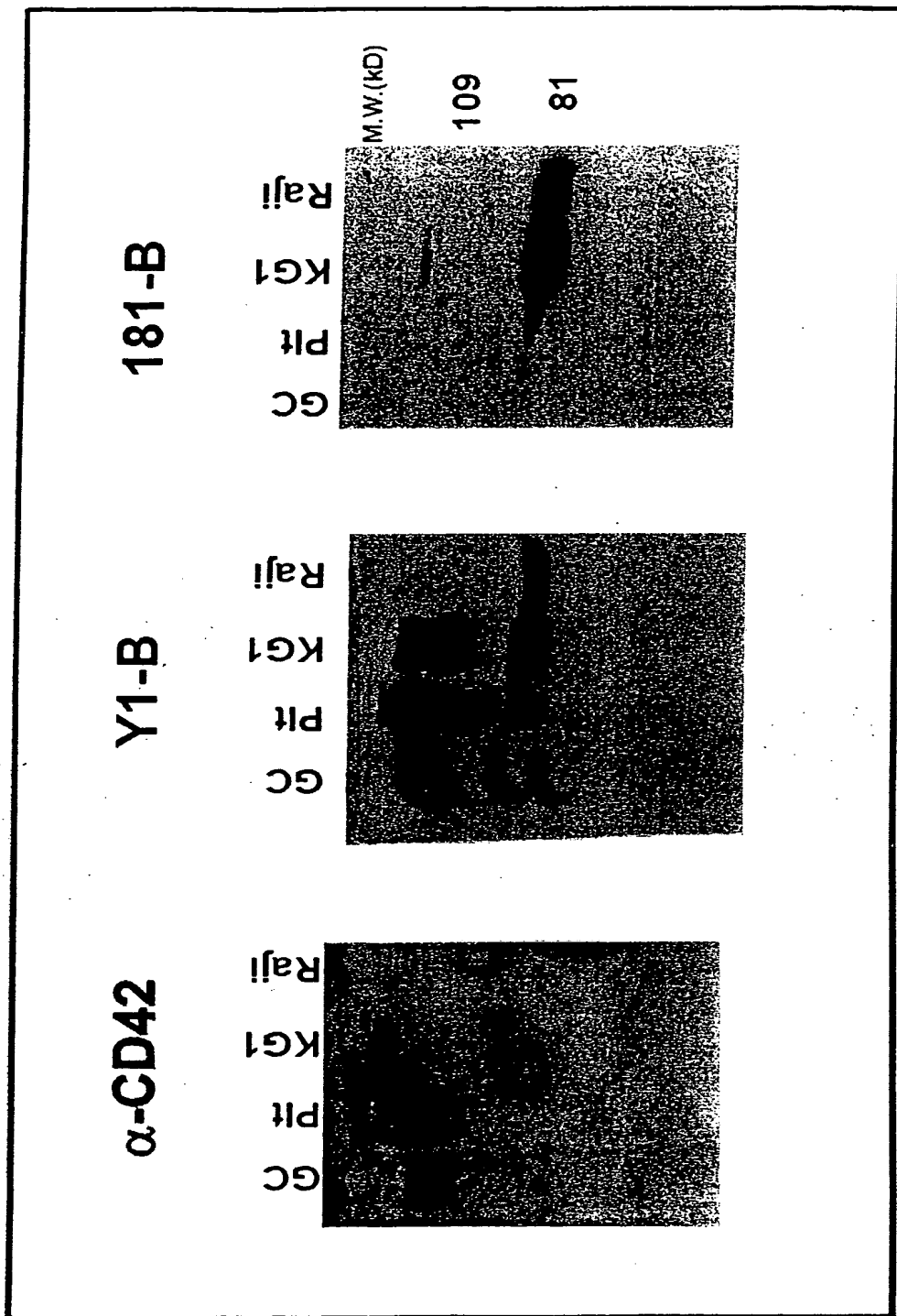
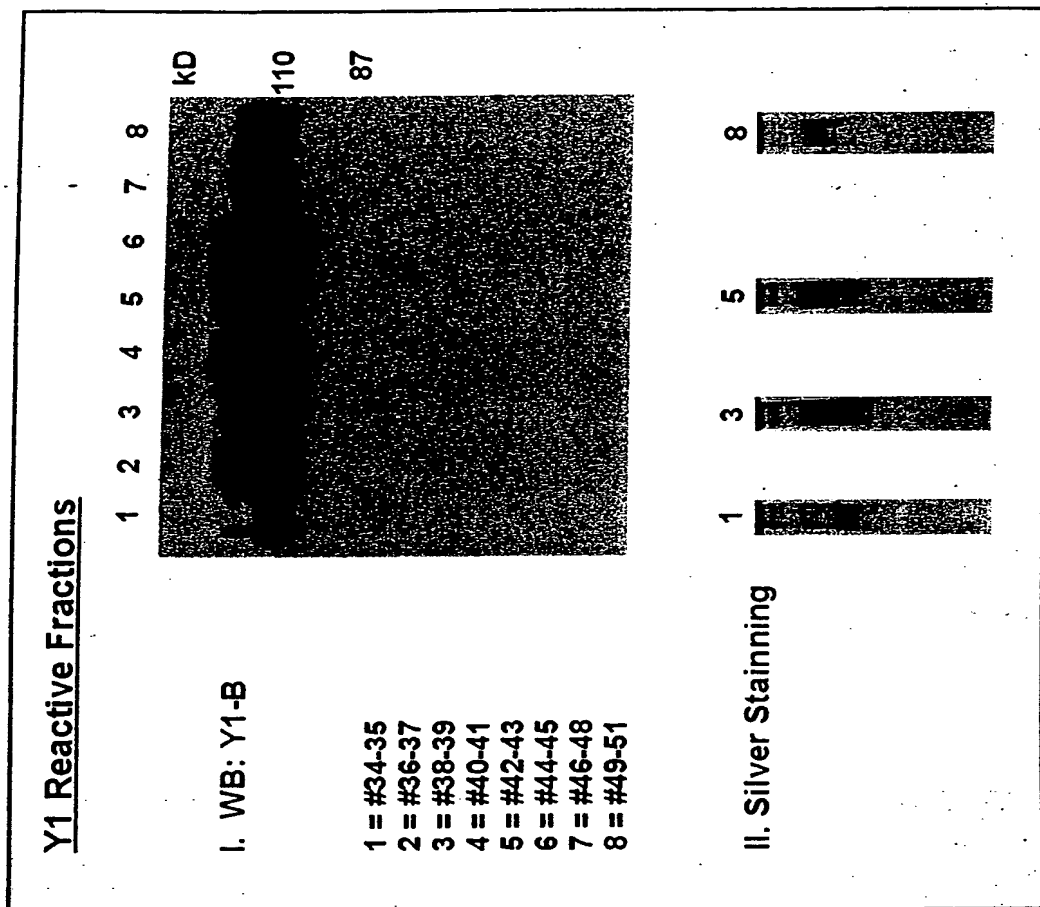




FIG. 21

Y1-Ligand from KG1 membranes following
Immuno-Precipitation with Y1:
Purification on RP-HPLC

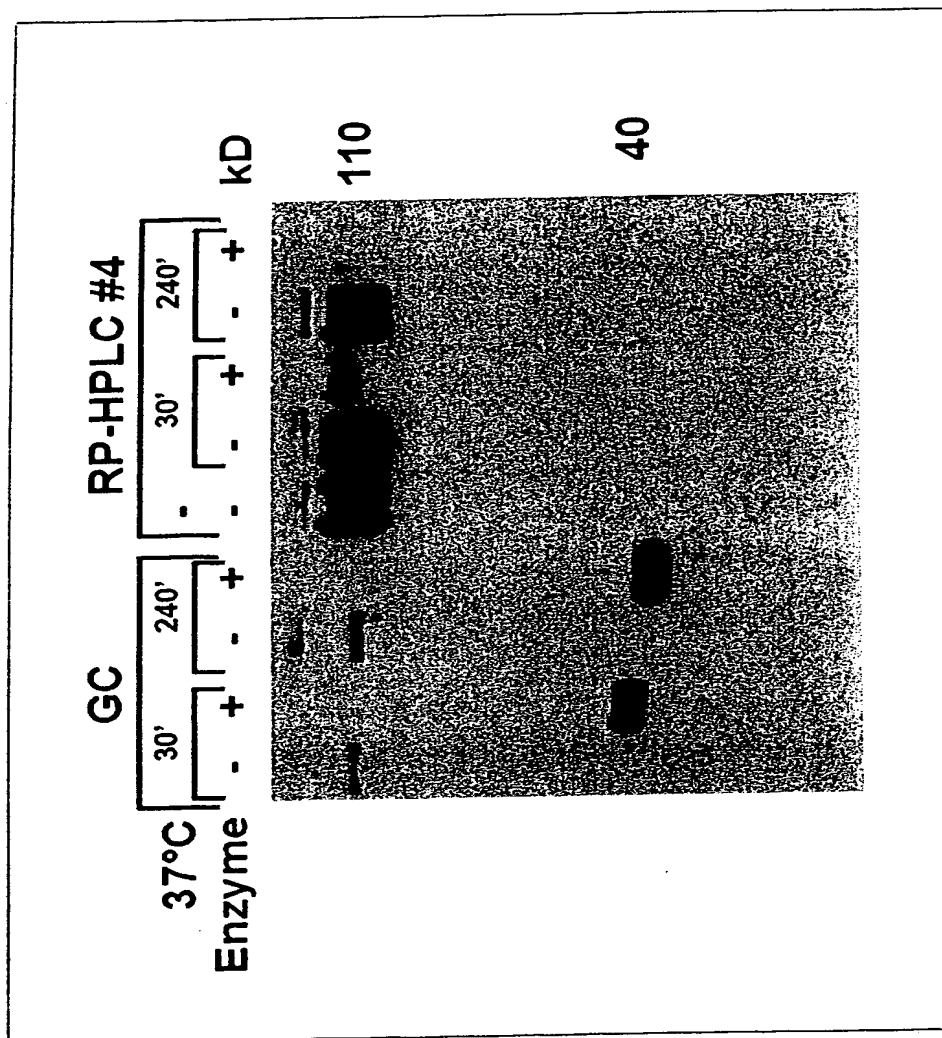




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FIG. 22

Effect of O-Sialo-Glycoprotein Endopeptidase on Y1 Binding



Effect of Aryl-Sulfatase on Binding of Y1: RP-HPLC(KG1) & H-B(Heparin-BSA)

Sulfatase
OS-Protase

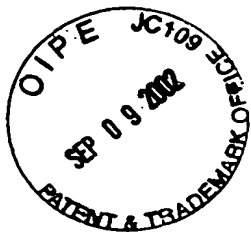
- + - + -
- - - - -

H-B	RP-HPLC
-----	---------

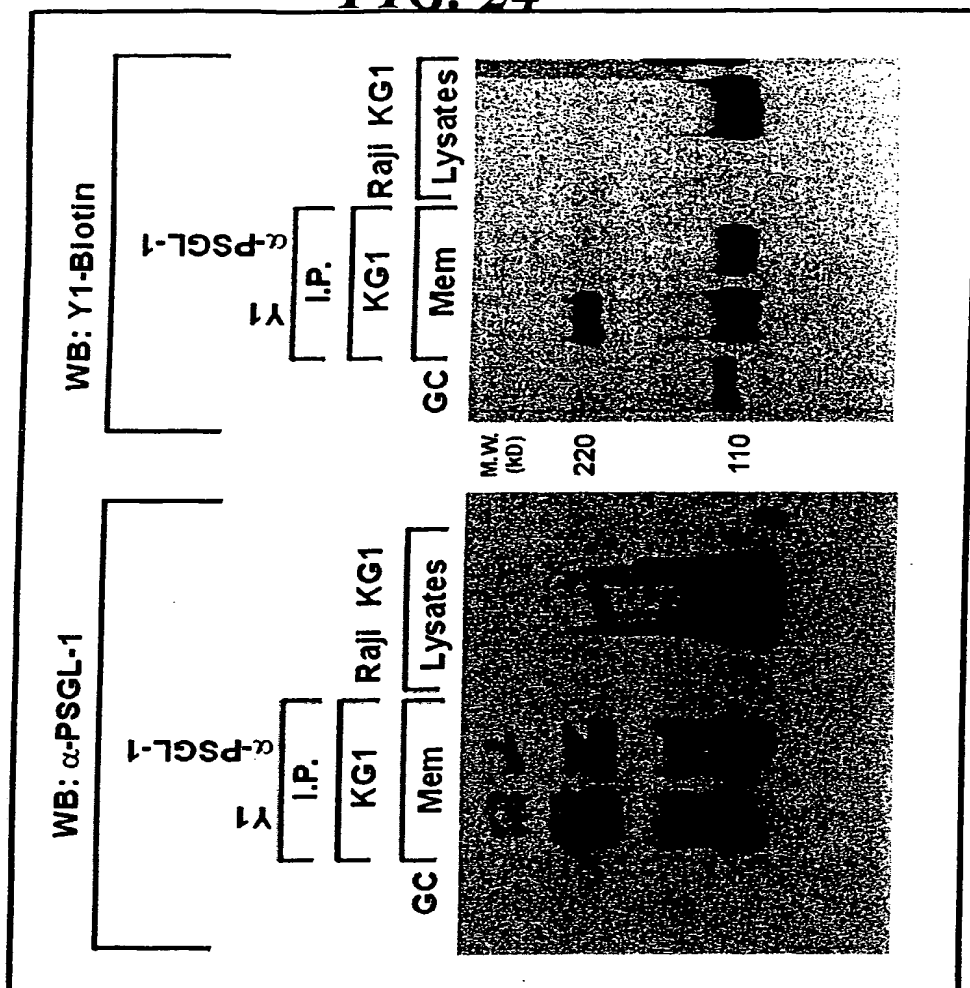
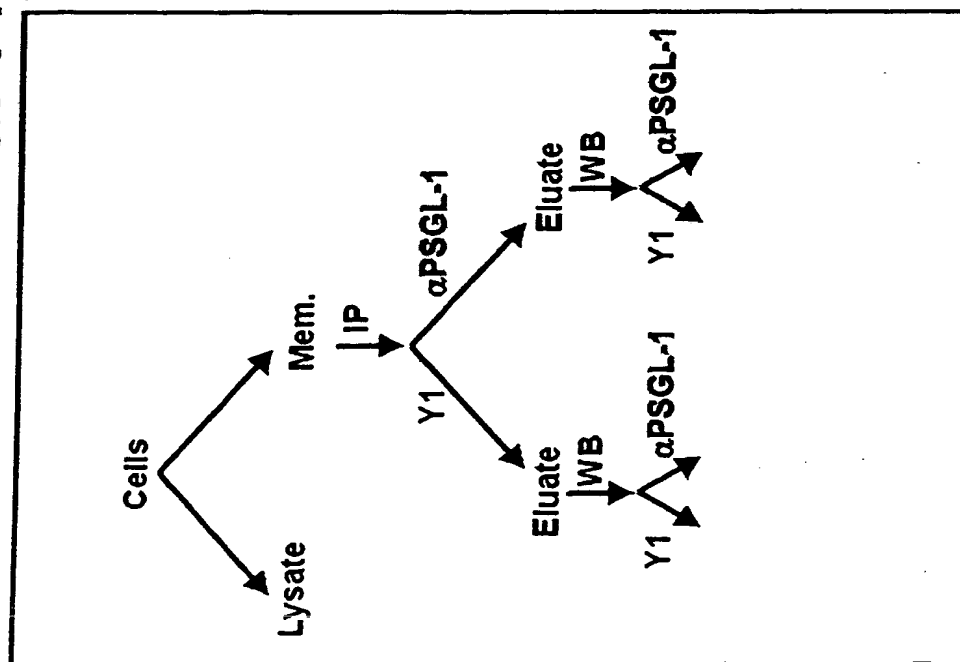


FIG. 23

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Specificity of Y1 Binding: Analysis by Immune Precipitation with Y1 and anti-PSGL-1



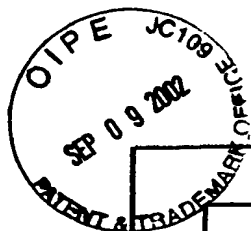
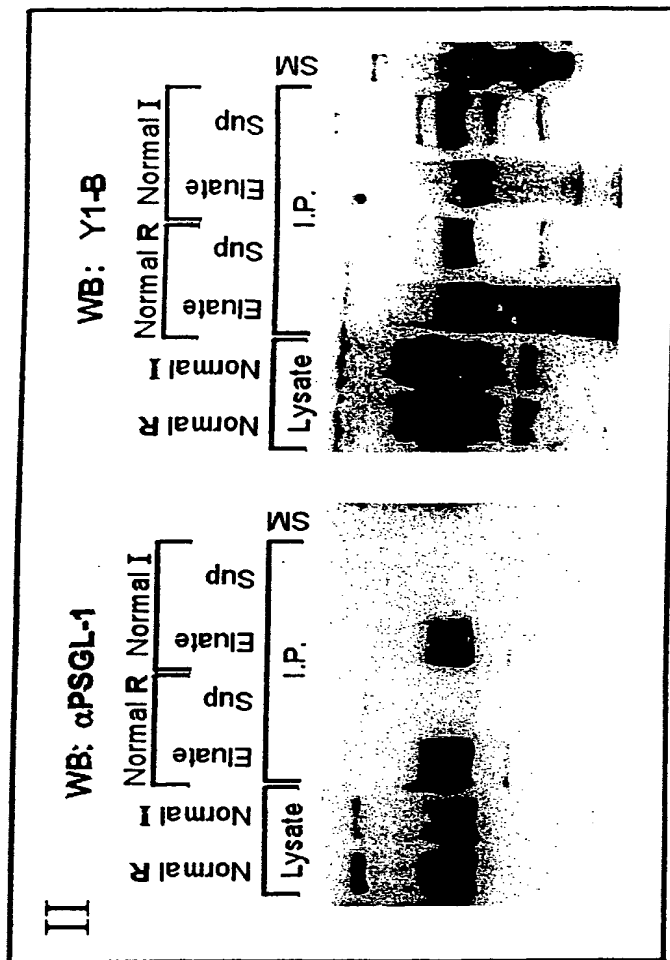
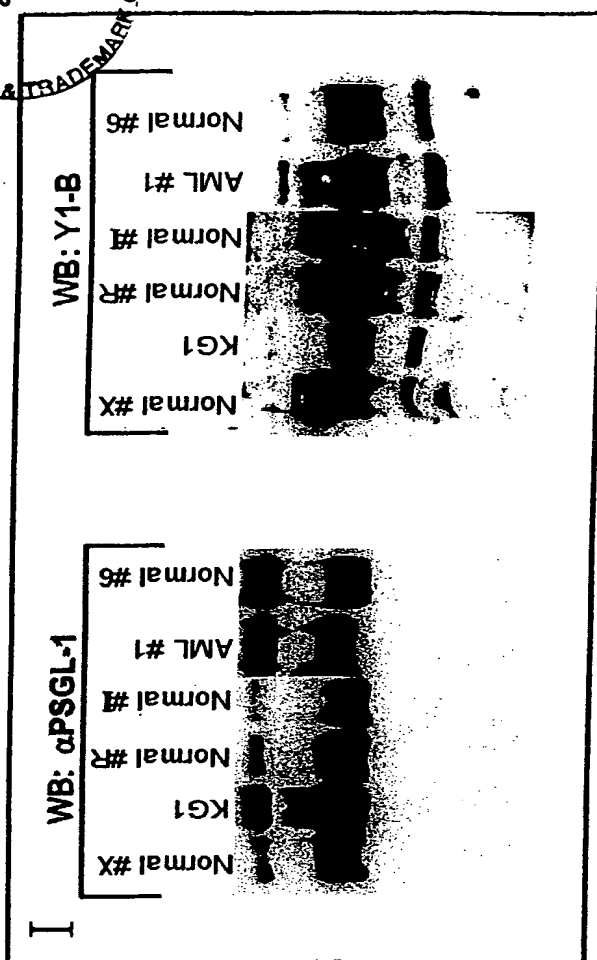
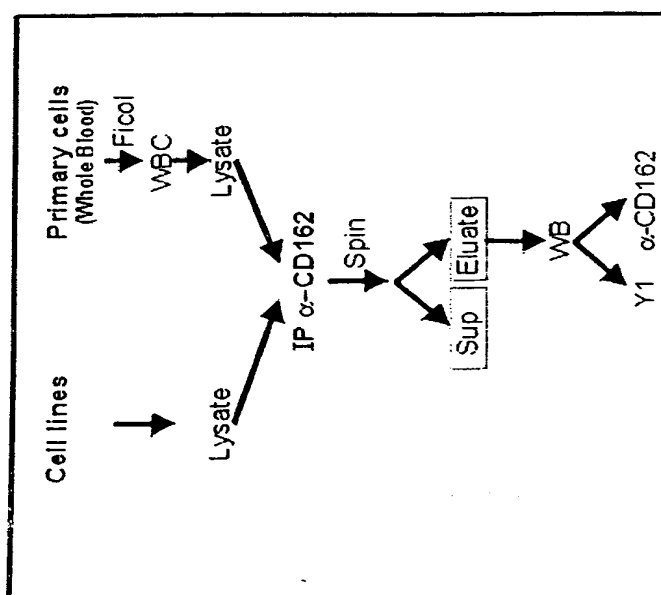
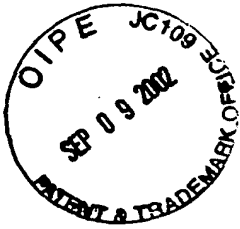


FIG. 25



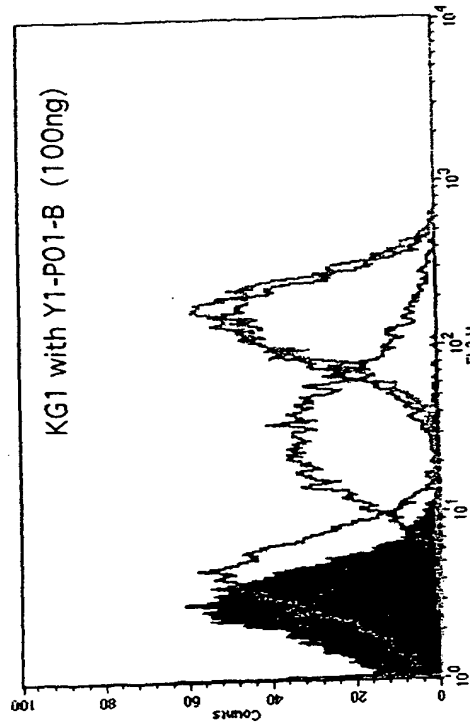
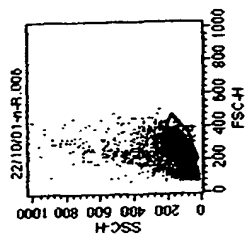
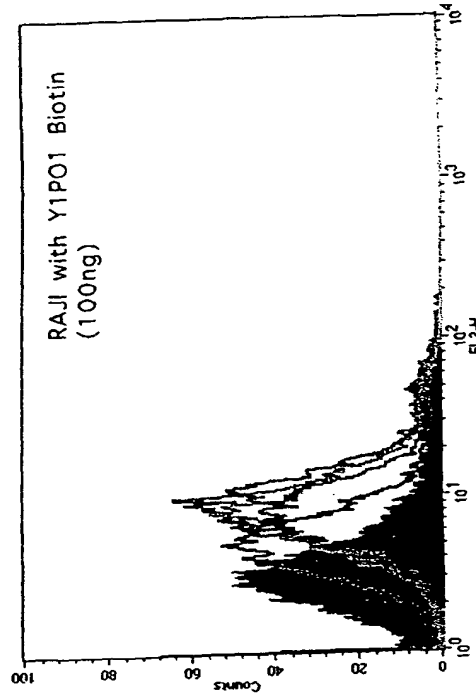
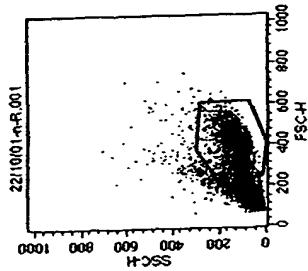
α-CD162 and Y1:
Comparison between cells
from AML patient and normal
blood



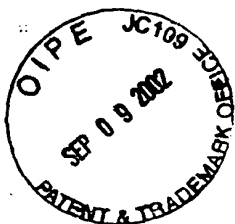


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FIG. 26



Key	Name	Parameter	Gate
■	22/1001-nR.006	N01-B	
—	22/1001-nR.007	P01-B	
—	22/1001-nR.008	+KPL1	
—	22/1001-nR.009	+PL1	
—	22/1001-nR.010	+PL2	

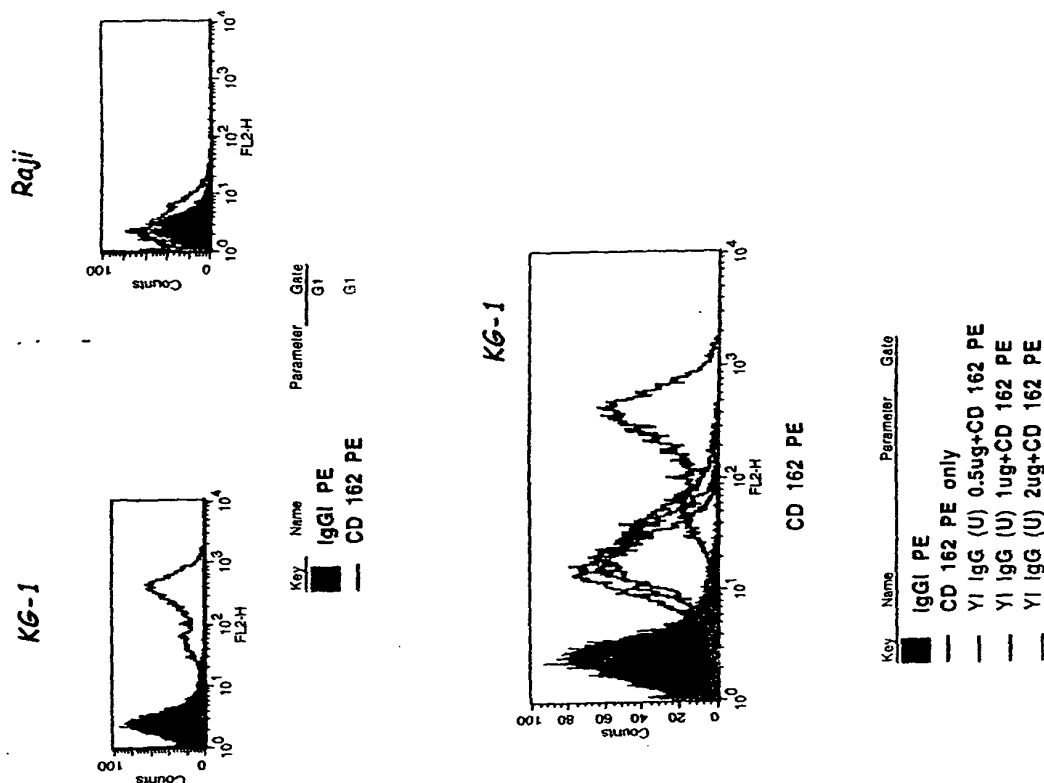


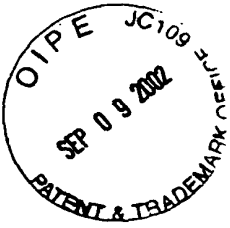
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FIG. 27

Specificity of Y1 Binding: Analysis by FACS

- Binding of
 α PSGL1
(α CD162/KPL1);
competition
with Y1-IgG





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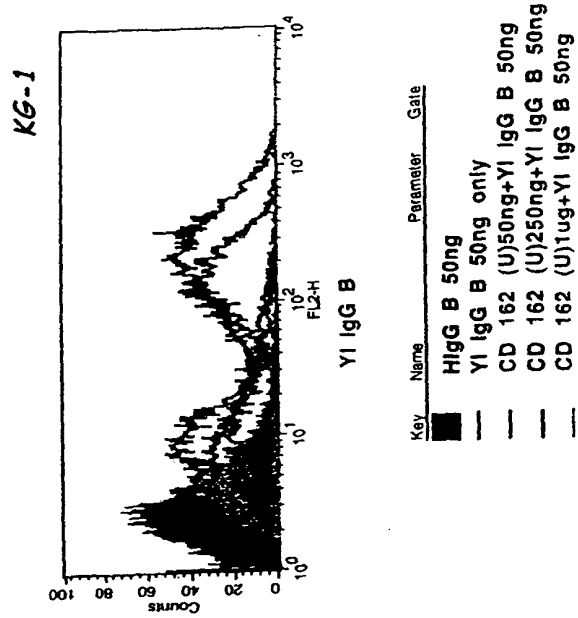
FIG. 28

Specificity of Y1 Binding: Analysis by FACS

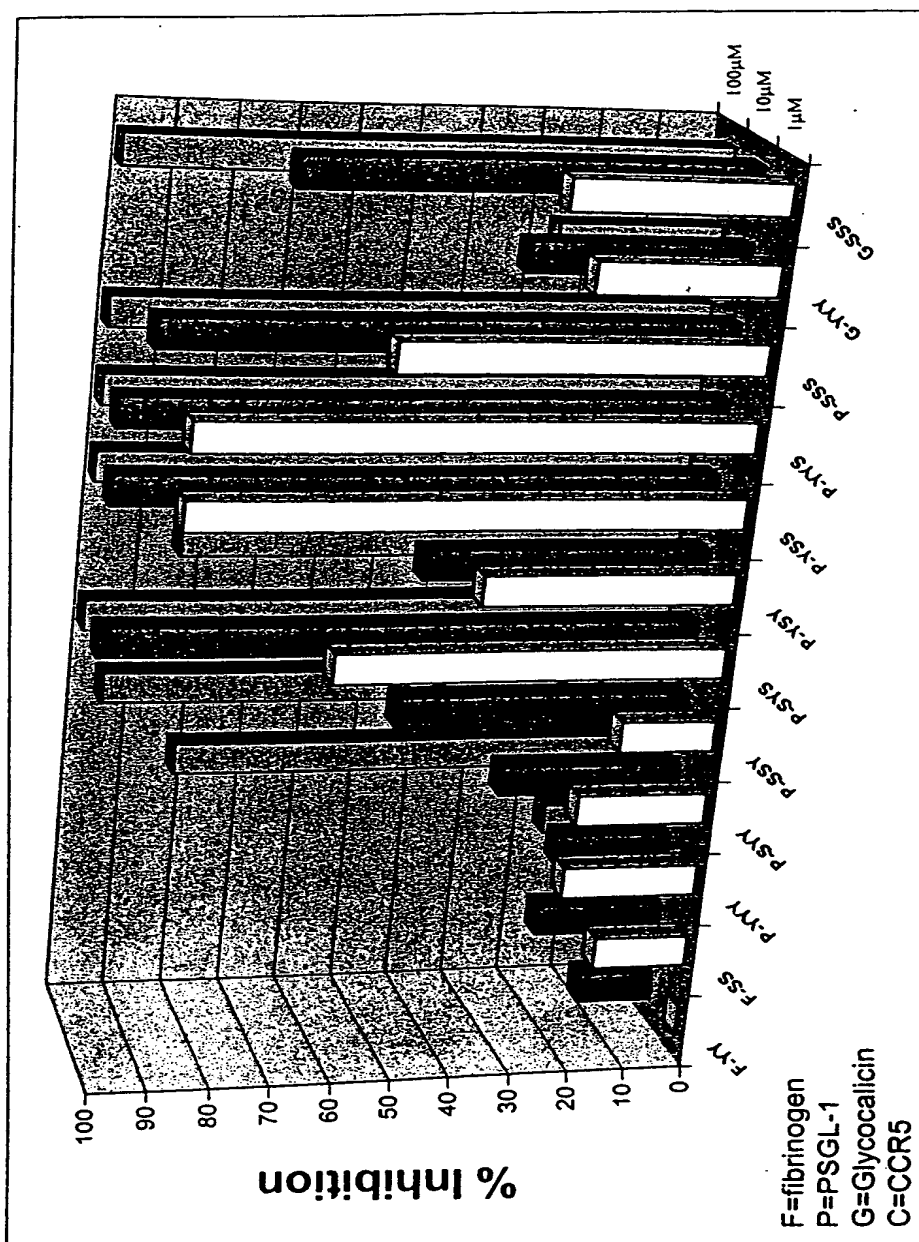


- Binding of Y1-IgG; competition with α PSGL-1 (CD162 /KPL1)

COMPETITION



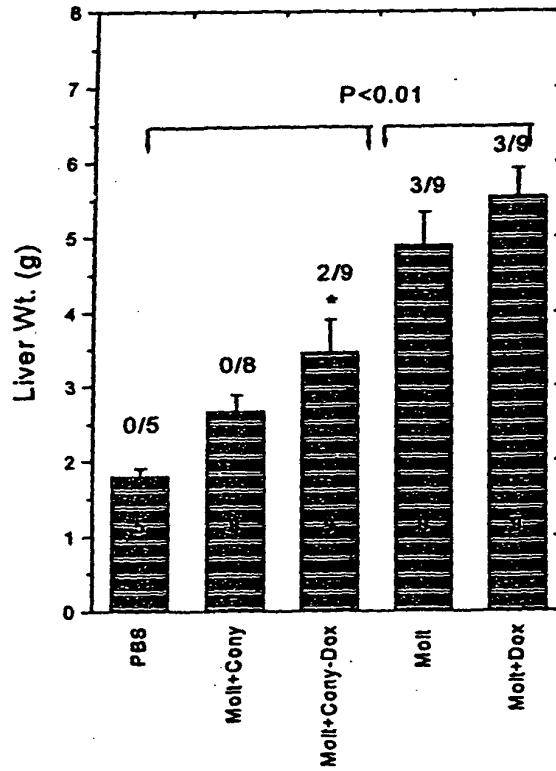
	F-YY	F-SS	P-YYY	P-SYY	P-SSY	P-SYS	P-YSY	P-YSS	P-YY'S	P-SSS	G-YYY	G-SSS
100μM	0	0	18	83	96	100	85	100	100	100	100	28
10μM	13	22	20	31	50	100	48	100	100	95	37	75
1μM	0	16	23	22	16	65	42	91	91	60	30	36

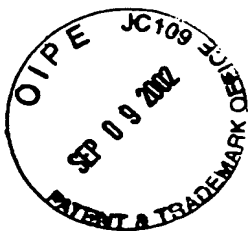




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FIG. 30

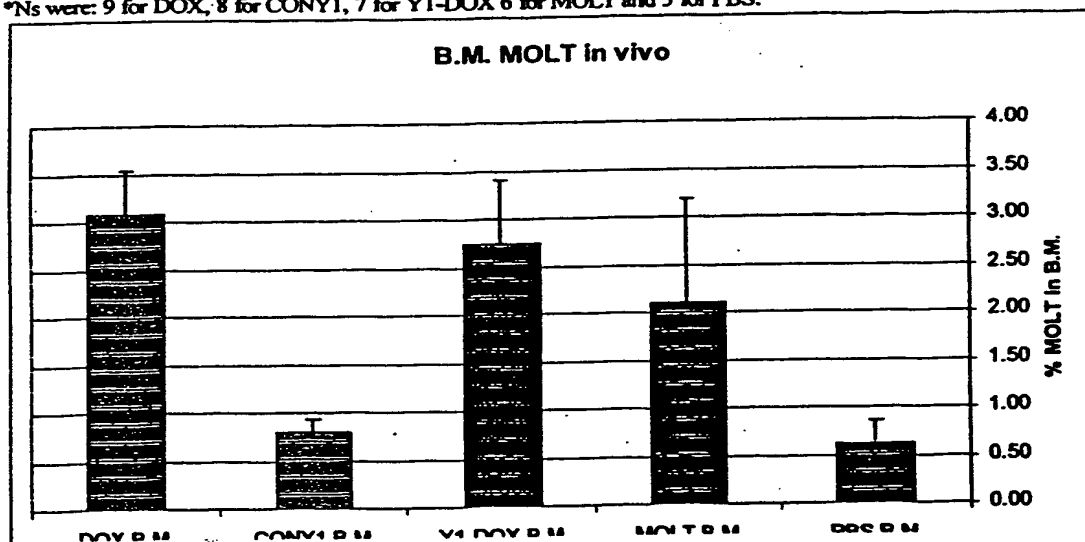


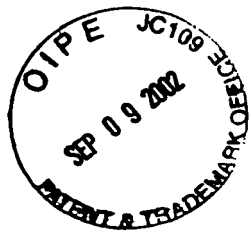


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FIG. 31

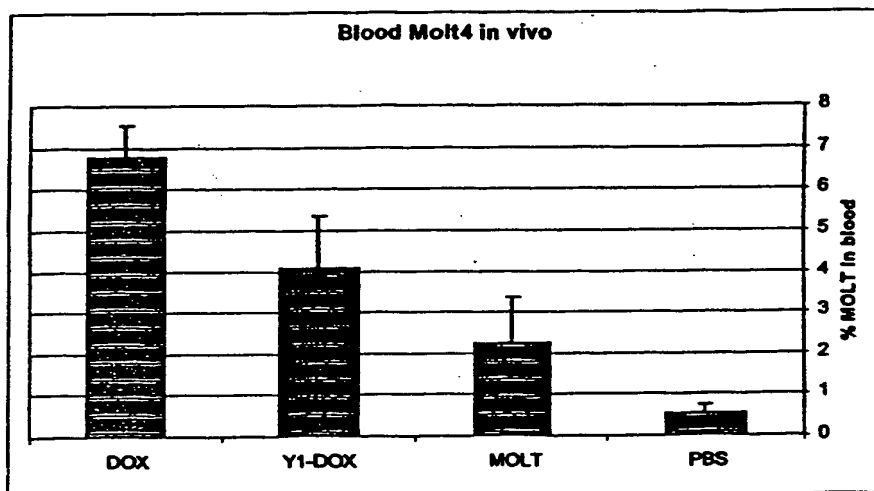
*Ns were: 9 for DOX, 8 for CONY1, 7 for Y1-DOX 6 for MOLT and 5 for PBS.





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FIG. 32

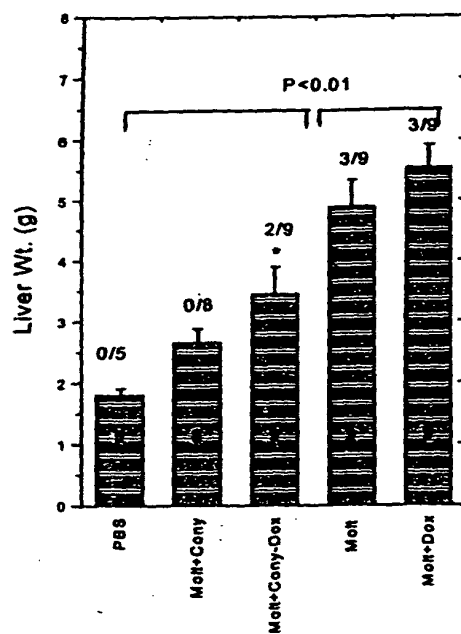


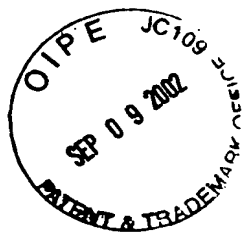
**Ns were: 4 for DOX, 2 for Y1-DOX, 3 for MOLT and 3 for PBS.

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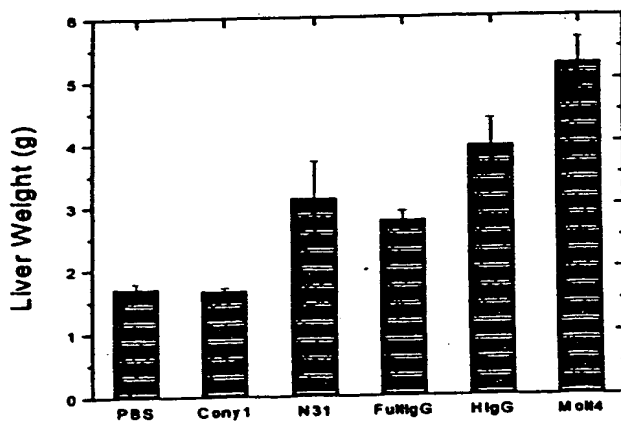
FIG. 33





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FIG. 34



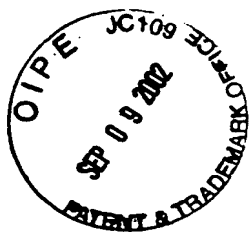
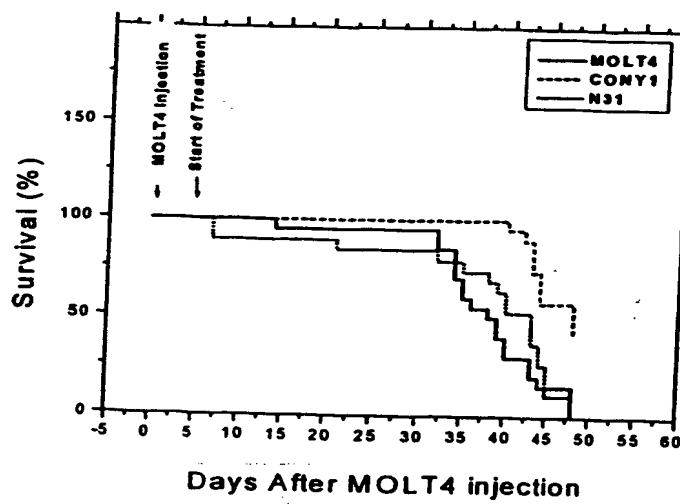
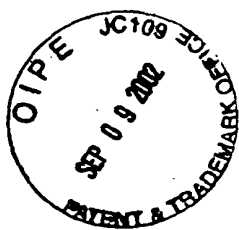


FIG. 35

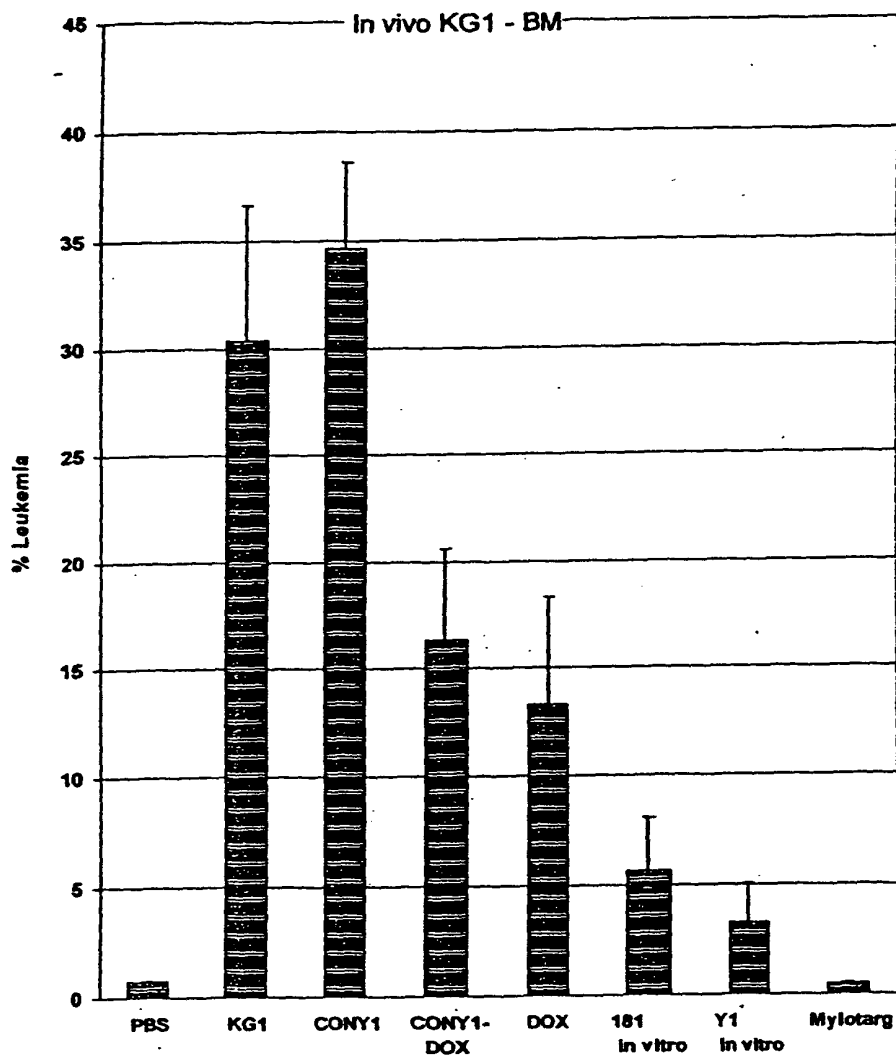


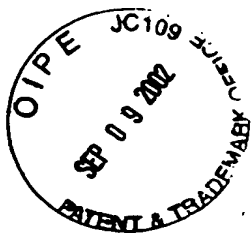


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FIG. 36

***Ns were: 8 for PBS, 9 for KG1, 8 for CONY1, 11 for CONY1-DOX, 9 for DOX, 8 for 181 in vitro, 9 for Y1 in vitro and 9 for Mylotarg.

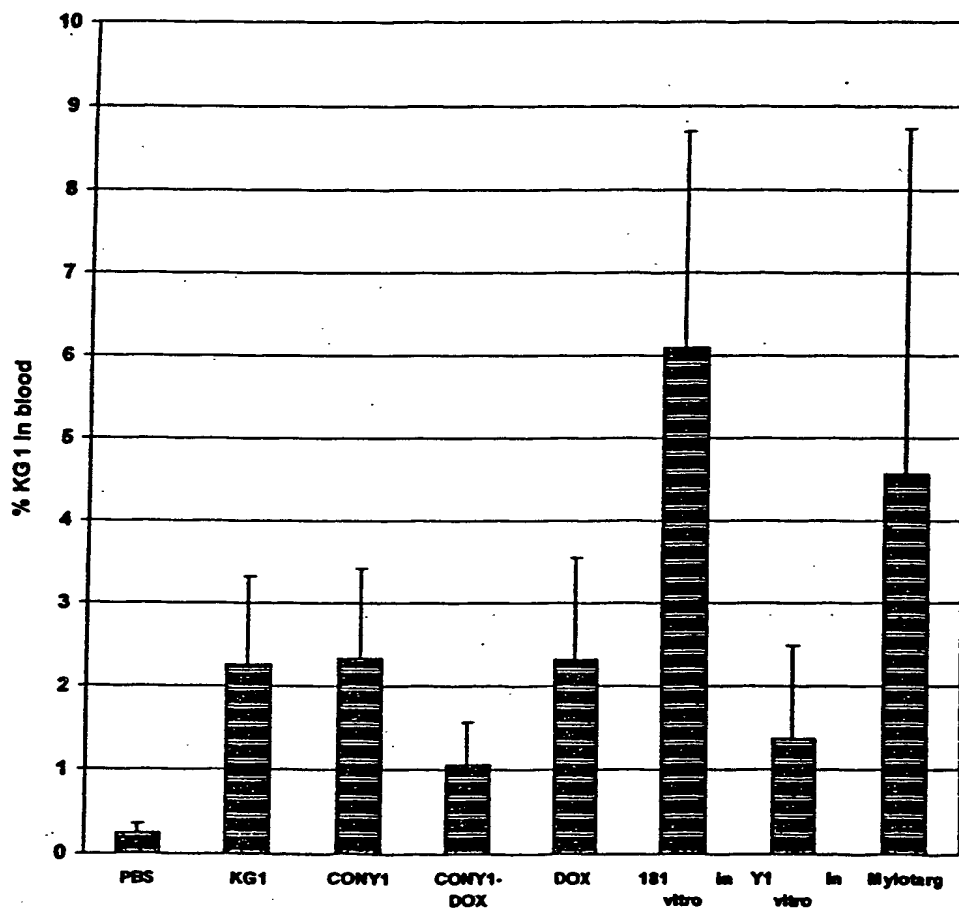




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FIG. 37

In vivo KG1 - Blood

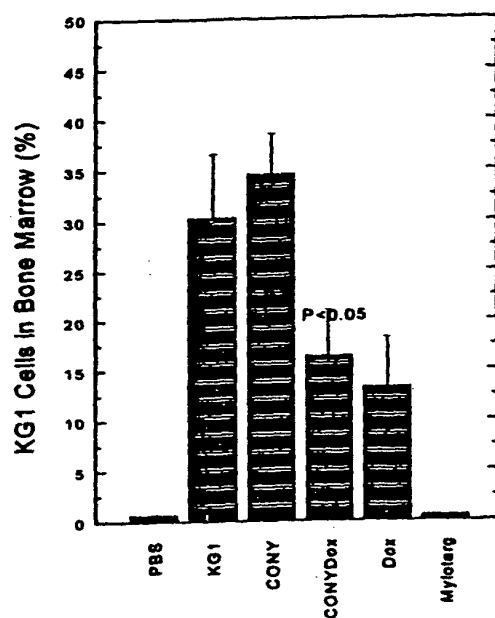


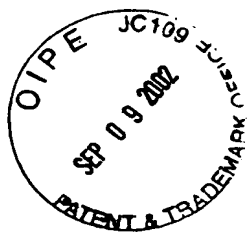
****Ns were: 8 for PBS, 9 for KG1, 8 for CONY1, 9 for CONY1-DOX, 11 for DOX (including one mice injected with 5mg/kg DOX), 7 for 181 in vitro, 8 for Y1 in vitro and 7 for Mylotarg.



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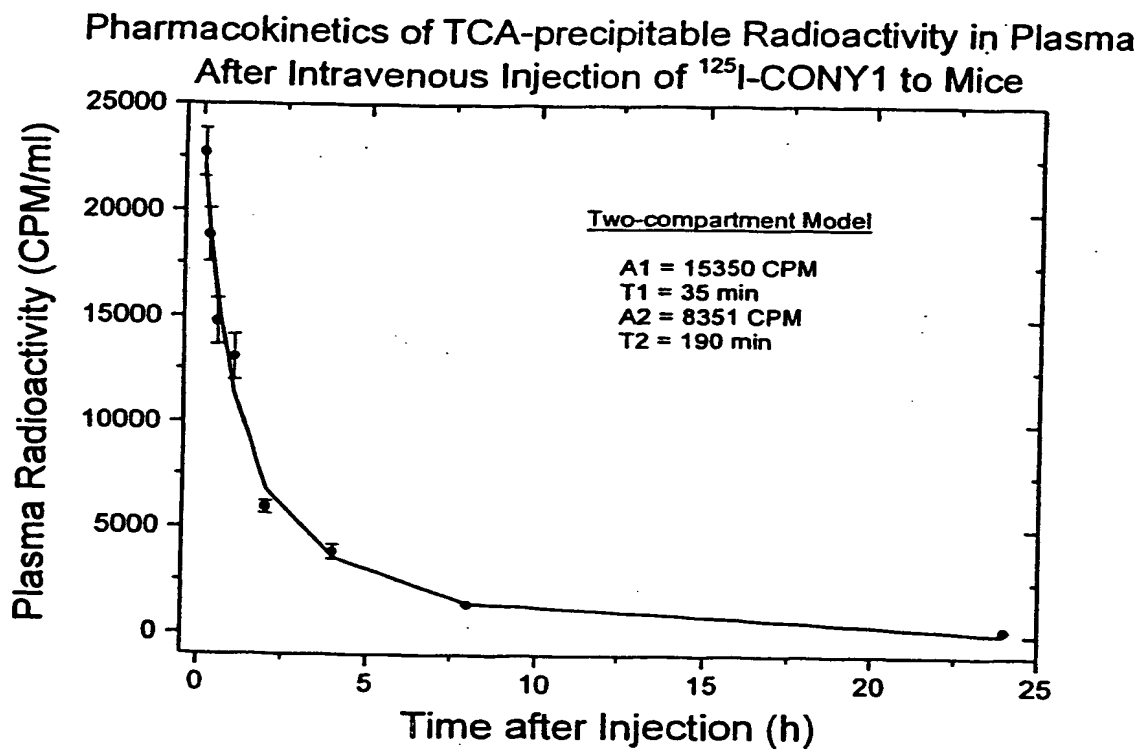
FIG. 38





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FIG. 39



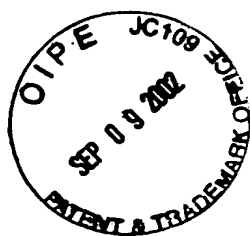
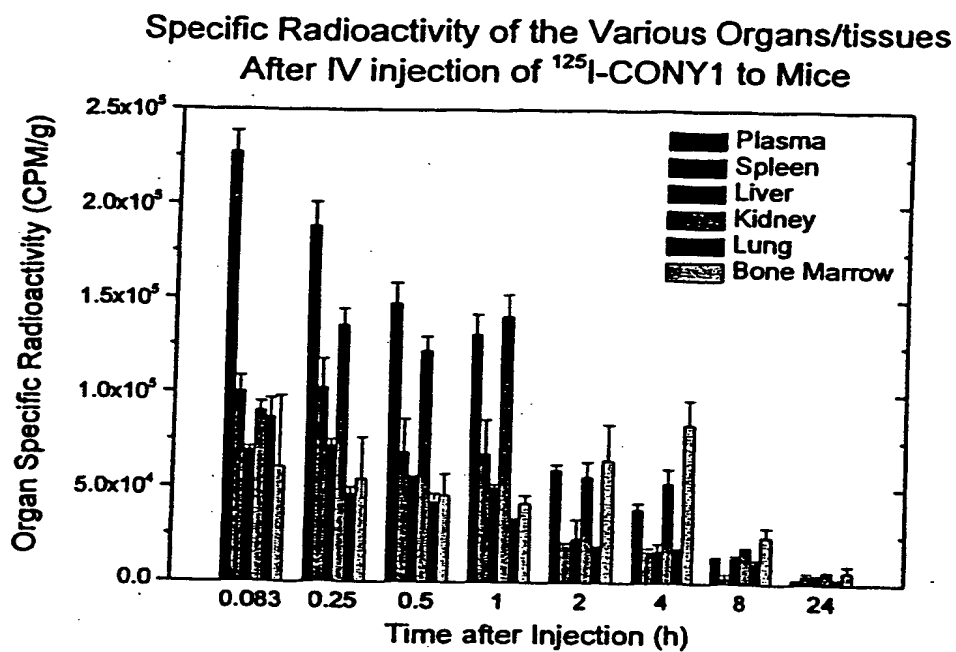
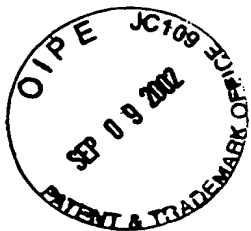


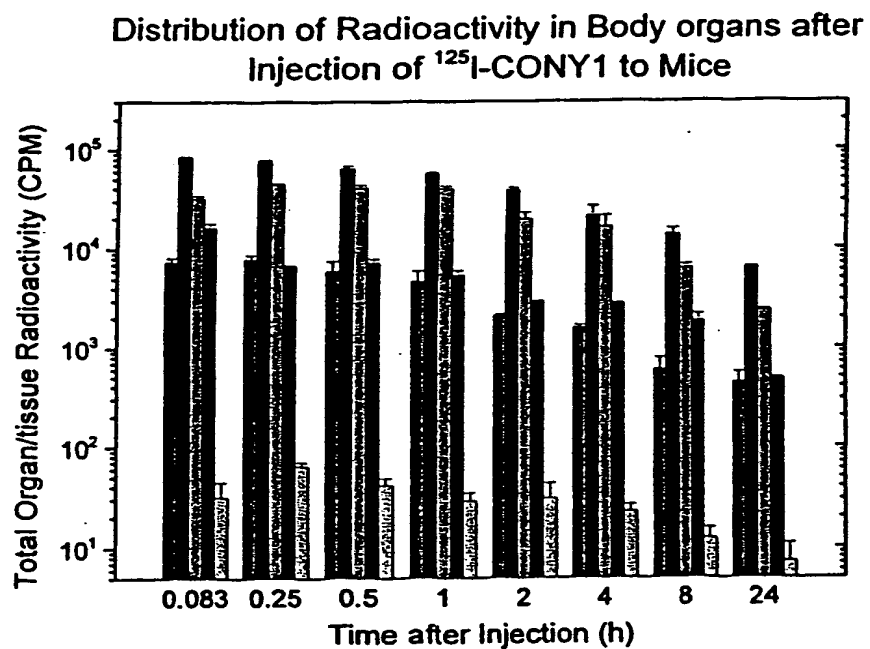
FIG. 40





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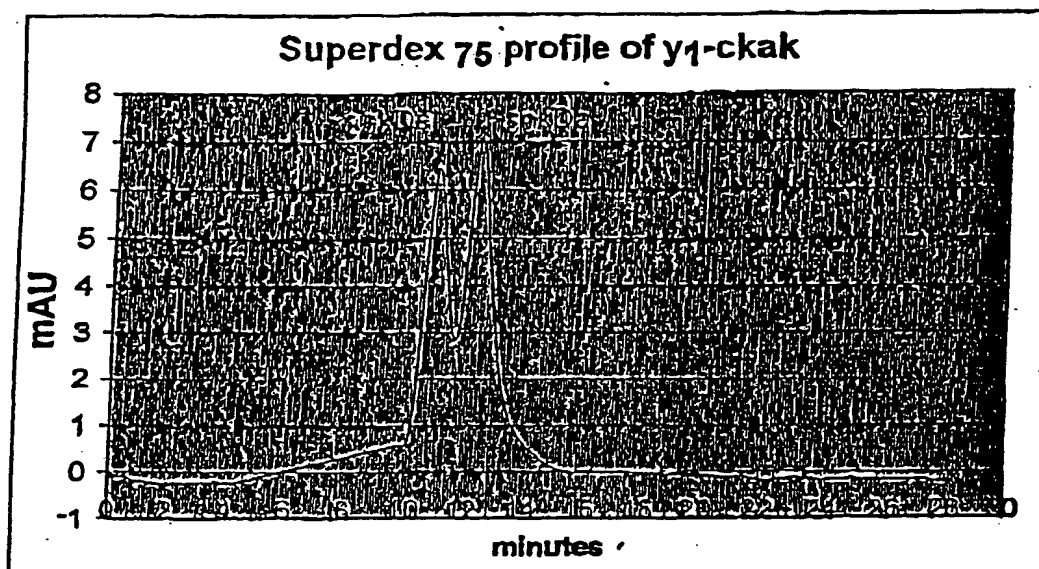
FIG. 41

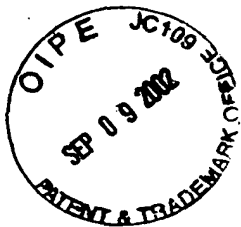




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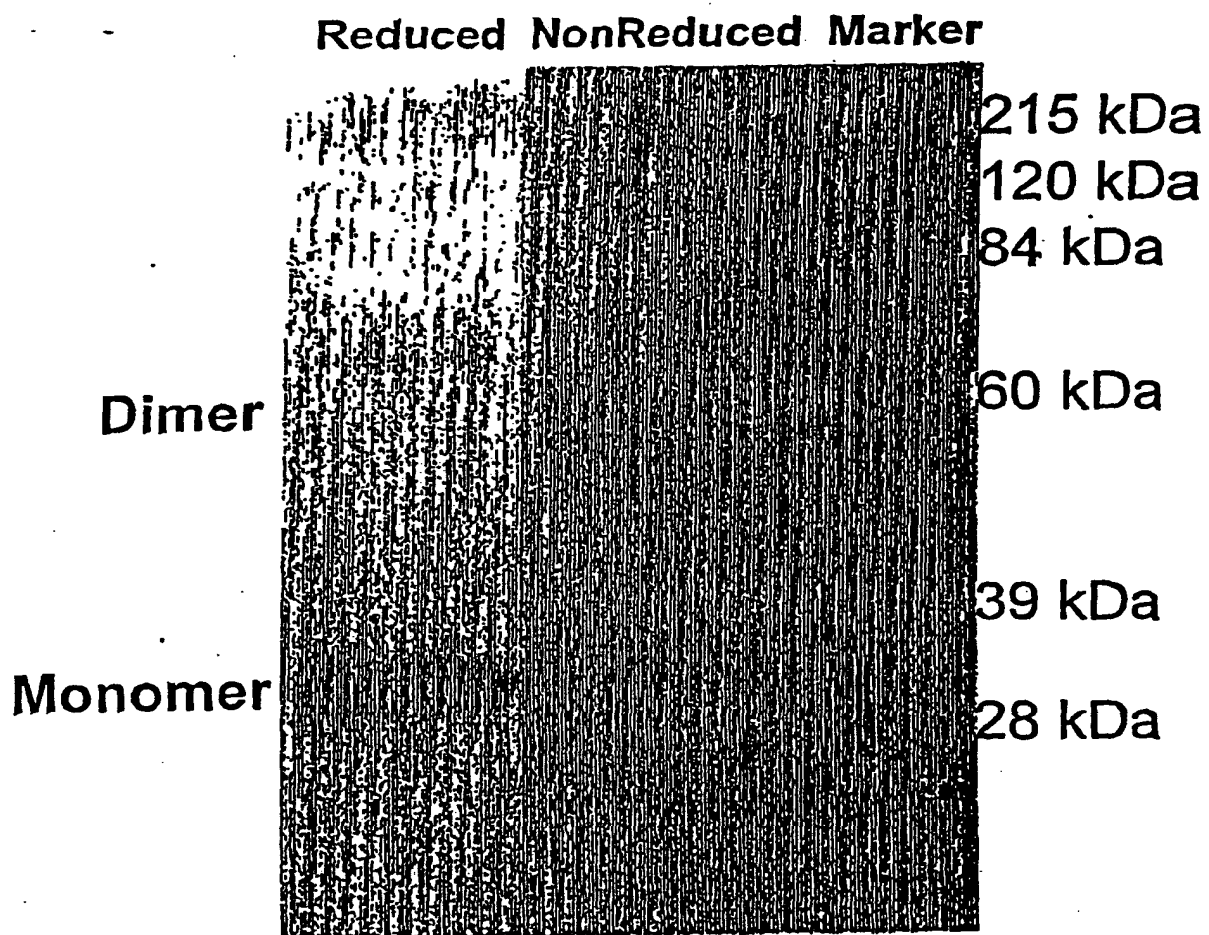
FIG. 42





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FIG. 43



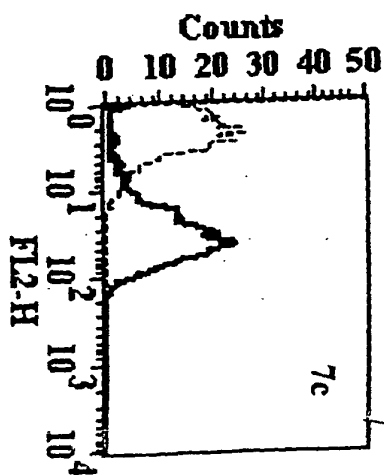
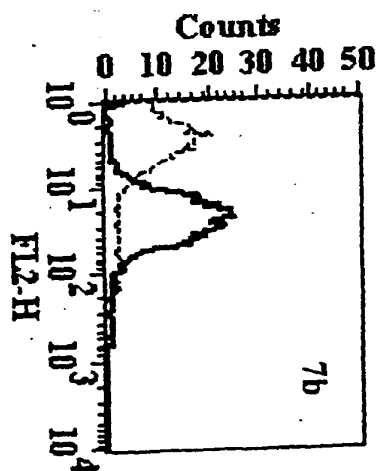
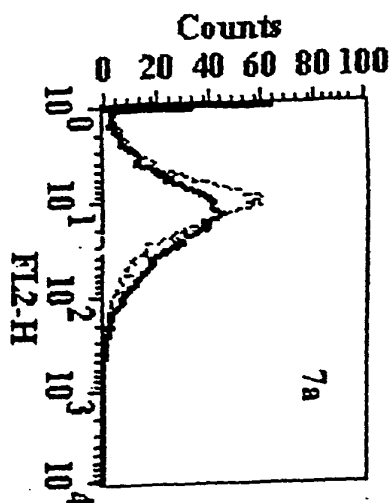


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FIG. 44

Control antibody

Y-1 antibody

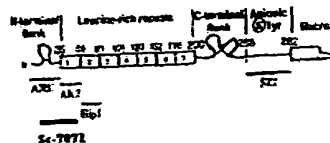
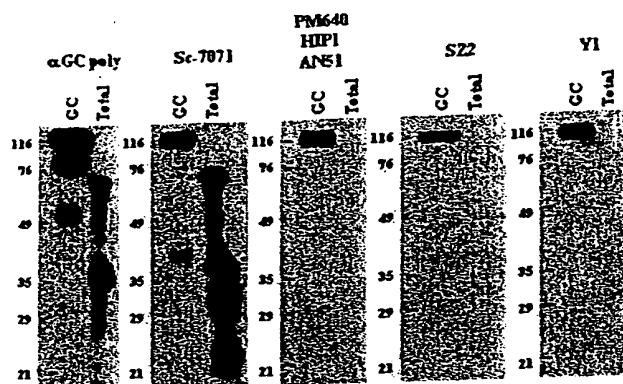


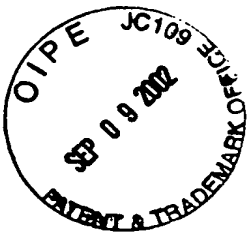


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FIG. 45

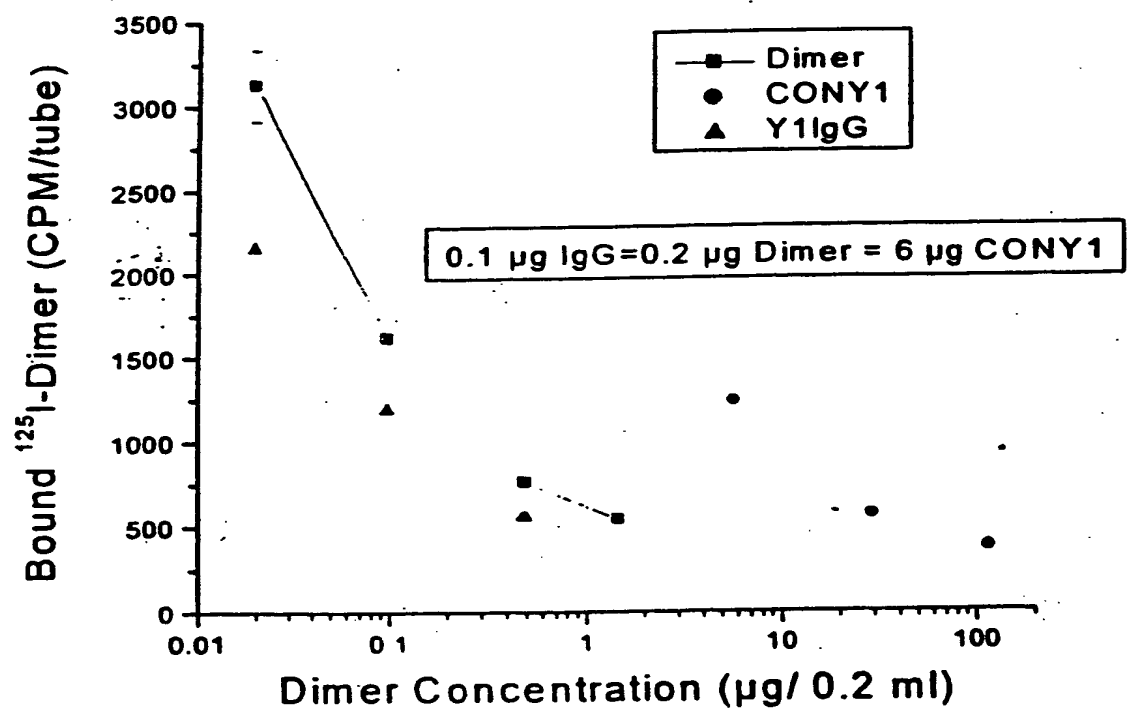
Epitopes of anti-GPIb α antibodies





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FIG. 46





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FIG. 47

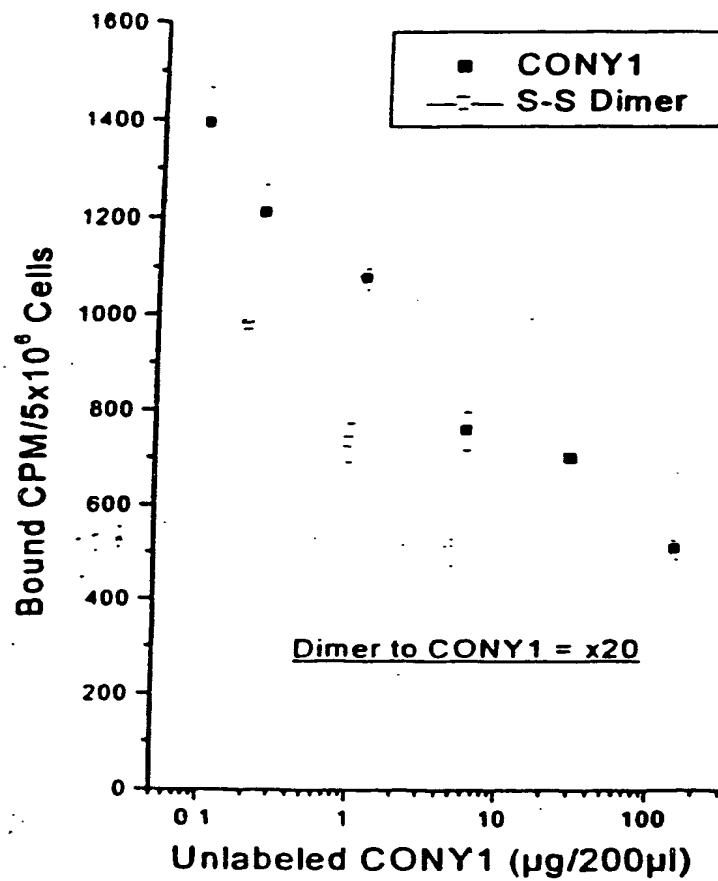




FIG. 48A: The ORF and Amino Acid Sequence of Y1-HC

SEQ ID NO: 205 (nucleic acid sequence): SEQ ID NO: 206 (amino acid sequence)

```

1      ATGGCCTGGGCTCTGCTGCTCCTOACCCTCCTCACTCAGGACACAGGGTCTGGGCCGAT
1      M A W A L L L L T L L T Q D T G S W A D
61     ATCCAGCTGGTGGAGTCTGGGGGAGGTGTGGTACGGCCTGGGGGGTCCCTGAGACTCTCC
21     I Q L V E S G G G V V R P G G S L R L S
121    TGTGCAGCCTCTGGATTACCTTTGATGATTATGGCATGAGCTGGGTCCGCCAAGCTCCA
41     C A A S G F T F D D Y G M S W V R Q A P
181    GGAAGGGGCTGGAGTGGGTCTCTGGTATTAATTGGAATGGTGGTAGCACAGGTTATGCA
61     G K G L E W V S G I N W N G G S T G Y A
241    GACTCTGTGAAGGGCCGATTACCATCTCTAGAGACAACGCCAAGAATCCCTGTATCTG
81     D S V K G R F T I S R D N A K N S L Y L
301 -  CAAATGAACAGTCTGAGAGCCGAGGACACGGCCGTGTATTACTGTGCAAGAATAGGGCT
101    Q M N S L R A E D T A V Y Y C A R M R A
361    CCTGTGATTTGGGGCCAAGGTACCCTGGTCACCGTCTCGAGTGCTTCCACCAAGGGCCCA
121    P V I W G Q G T L V T V S S A S T K G P
421    TCGGTCTTCCCCCTGGCACCTCTCCAAGAGCACCTCTGGGGGCACAGCGGCCCTGGGC
141    S V F P L A P S S K S T S G G T A A L G
481    TGCCTGGTCAAGGACTACTTCCCCGAACCGGTGACGGTGTCTGTGGAATCAGGCGCCCTG
161    C L V K D Y F P E P V T V S W N S G A L
541    ACCAGCGCGTGCACACCTTCCCGGTGTCTACAGTCTCAGGACTCTACTCCCTCAGC
181    T S G V H T F P A V L Q S S G L Y S L S
601    AGCGTGGTGACCGTGCCCTCCAGCAGCTTGGGCACCCAGACCTACATCTGCAACGTGAAT
201    S V V T V P S S S L G T Q T Y I C N V N
661    CACAAGCCCAGCAACACCAAGGTGGACAAGAGAGTTGAGCCCAAACTCTTGACAAAAT
221    H K P S N T K V D K R V E P K S C D K T
721    CACACATGCCACCGTGCCAGCACCTGAACTCCTGGGGGGAGTGTGAGTCTTCTCTTC
241    H T C P P C P A P E L L G G P S V F L F
781    CCCCCAAACCAAGGACACCTCATGATCTCCCGGACCCCTGAGGTACATGCGTGGT
261    P P K P K D T L M I S R T P E V T C V V
841    GTGGACGTGAGCCACGAAGACCTGAGGTCAAGTTCAACTGGTACGTGGACGGCGTGGAG
281    V D V S H E D P E V K F N W Y V D G V E
901    GTGCATAATGCCAAGACAAAGCCGCGGGAGGAGCAGTACAACAGCACGTACCGTGTGGTC
301    V H N A K T K P R E E Q Y N S T Y R V V
961    AGCGTCTCACCCTCTGCACCAAGGACTGGCTGAATGGCAAGGAGTACAAGTGAAGGTC
321    S V L T V L H Q D W L N G K E Y K C K V
1021   TCCAACAAAGCCCTCCCAGCCCCATCGAGAAAACCATCTCAAAGCCAAAGGGCAGCCC
341    S N K A L P A P I E K T I S K A K G Q P
1081   OGAGAACCACAGGTGTACACCTGCCCCCATCCCGGAGGAGATGACCAAGAACCAGGTC
361    R E P Q V Y T L P P S R E E M T K N Q V
1141   AGCCTGACCTGCCTGGTCAAAGGCTTCTATCCCAGCGACATCGCCGTGGAGTGGGAGAGC
381    S L T C L V K G F Y P S D I A V E W E S
1201   AATGGGCAGCCGAGACAACACTACAAGACCACGTCTCCCGTGTGACTCCGACGGCTCC
401    N G Q P E N N Y K T T S P V L D S D G S
1261   TTCTTCCTCTATAGCAAGCTCACCGTGCACAAGAGCAGGTGGCAGCAGGGGAACTCTTC
421    F F L Y S K L T V D K S R W Q Q G N V F
1321   TCATGCTCCGTGATGCATGAGGCTCTGCACAACCACTACACGCAGAAGAGCCTCTCCCTG
441    S C S V M H E A L H N H Y T Q K S L S L
1381   TCTCTGGGTAAATGA
461    S L G K *

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FIG. 48B: The ORF and Amino Acid Sequence of Y1-LC

SEQ ID NO: 207 (nucleic acid sequence); SEQ ID NO: 208 (amino acid sequence)

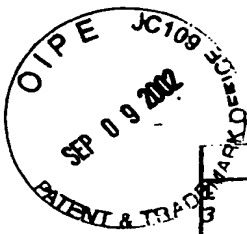
1	ATGGCCTGGGCTCTGCTGCTCCTCACCTCCTCACTCAGGACACAGGGTCTGGGCCGAT
1	<u>M A W A L L L L T L L T Q D T G S W A D</u>
61	GCAGAGCTGACTCAGGACCCTGCTGTGTCTGTGGCCTTGGGACAGACAGTCAGGATCACA
21	A E L T Q D P A V S V A L G Q T V R I T
1212	TGCCAAGGAGACAGCCTCAGAAGCTATTATGCAAGCTGGTACCAGCAGAAGCCAGGACAG
41	C Q G D S L R S Y Y A S W Y Q Q K P G Q
181	GCCCCTGTACTTGTCTATCTATGGTAAAAACAACCGGCCCTCAGGGATCCCAGACCGATT
161	A P V L V I Y G K N N R P S G I P D R F
241	TCTGGCTCCAGCTCAGGAAACACAGCTTCCTTGACCATCACTGGGGCTCAGGCGGAAGAT
81	S G S S S G N T A S L T I T G A Q A E D
301	GAGGCTGACTATTACTGTAACTCCCGGGACAGCAGTGGTAACCATGTGGTATTTCGGCGGA
101	E A D Y Y C N S R D S S G N H V V F G G
361	GGGACCAAGCTGACCGTCTTAGGTCAGCCCAAGGCTGCCCCCTCGGTCACTCTGTTC
121	G T K L T V L G Q P K A A P S V T L F P
421	CCCTCCTCTGAGGAGCTTCAAGCCAACAAGGCCACACTGGTGTGTCTCATAAGTGACTTC
141	P S S E E L Q A N K A T L V C L I S D F
481	TACCCGGGAGCCGTGACAGTGGCCTGGAAGGCAGATAGCAGCCCCGTCAAGGCGGGAGTG
161	Y P G A V T V A W K A D S S P V K A G V
541	GAGACCACACACCTCCAAACAAAGCAACAACAAGTACGCGGCCAGCAGCTACCTGAGC
181	E T T T P S K Q S N N K Y A A S S Y L S
601	CTGACGCCTGAGCAGTGAAGTCCCAAAAAGCTACAGCTGCCAGGTACGCATGAAGGG
201	L T P E Q W K S H K S Y S C Q V T H E G
661	AGCACCGTGGAGAAGACAGTGGCCCCCTACAGAATGTTTCATGA
221	S T V E K T V A P T E C S *



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FIG. 49

1	11	21	31	41	51	
1	EVQLVESGGG	LVQPGGSLRL	SCAASGFTFS	SYAMSWVROA	PGKGLEWVSA	ISGSGGSTYY 60
61	ADSVKGRFTI	SRDNSKNTLY	LQMNSLRAED	TAVYYCARVA	KTLMRQYSLW	GQGTLVTVSR 120
121	GGGSGGGGGS	GGGGSSELTO	DPAVSVALGQ	TVRITCQGDS	LRSYIASWYQ	QKPGQAPVLV 180
181	IYGKNNRPSG	IPDRFSGSSS	GNTASLTITG	AQAEDADYY	CNSRDSSGNH	VVFSGGTKLT 240
241	VLGAAAEQKL	ISEEDLNGAA				

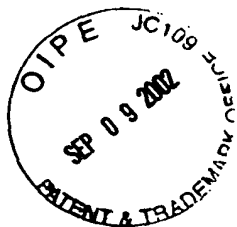


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FIG. 50

	10	20	30	40	50	60
1	AttTATTACTC	gCGGCCCCAGC	CgGCCCGGCG	CGAGGTGCAG	CTGGTGGAGT	CTGGGGGAGG
3	L L L A A Q P A M A	E V Q L V E S G G G				
	70	80	90	100	110	120
1	CTTGGTACAG	CCTGGGGGGT	CCTGAGACT	CTCTGTGCA	GCCTCTGGAT	TCACCTTTAG
3	L V Q P G G S L R L	S C A A S G F T F S				
	130	140	150	160	170	180
1	CAGCTATGCC	ATGAGCTGGG	TCCGCCAGGC	TCCAGGGAAG	GGCTGGAGT	GGGTCTCAGC
3	S Y A M S W V R Q A	P G K G L E W V S A				
	190	200	210	220	230	240
1	TATTAGTGGT	AGTGGTGGTA	GCACATACTA	CGCAGACTCC	GTGAAGGGCC	GGTTCACCAT
3	F S G S G G S T Y Y	A D S V K G R F T I				
	250	260	270	280	290	300
1	CTCCAGAGAC	AATCCCAAGA	ACACGCTGTA	TCTGCAATG	AACAGCCTGA	GAGCGAGGA
3	S R D N S K N T L Y	L Q M N S L R A E D				
	310	320	330	340	350	360
1	CACGGCGGTG	TATTACTGTG	CAAGACCGCG	GCAGAGTTT	TAAGCTTATG	GGGGCCAGG
3	T A V Y Y C A R T G	Q S I K R S W G Q G				
	370	380	390	400	410	420
1	TACCTGGTTC	ACCGTGTGGA	GAGGTGGAGG	CGGTTCAgGC	GGAgGTGgCT	CTGGCGGTGG
3	T L V T V S R G G G	G S G G G G S G G G				
	430	440	450	460	470	480
1	CGGATOGTCT	GAGCTGACTC	AGGACCCCTGC	TGTGTCTGTG	GCCTTGGGAC	AGACAGTCAG
3	G S S E L T Q D P A	V S V A L G Q T V R				
	490	500	510	520	530	540
1	GATCAGATGC	CAAGGAgACA	GCCTCAGAGG	CTATTATGCA	AGCTGGTACC	AGCAGAAGCC
3	I T C Q G D S L R S	Y Y A S W Y Q Q K P				
	550	560	570	580	590	600
1	AGGACAGGCC	CCTGTACTTG	TCATCTATGG	TAAAAACAAC	CGGCCCTCAG	GGATCCCAGA
3	G Q A P V L V I Y G	K N N R P S G I P D				
	610	620	630	640	650	660
1	CCGATTCTCT	GGCTCCAGCT	CAGGAACAC	AGCTTCCTTG	ACCATCACTG	GGGCTCAGGC
3	R F S G S S S G N T	A S L T I T G A Q A				
	670	680	690	700	710	720
1	GGAAGATGAG	GCTGACTATT	ACTGTAACTC	CGGGGACAGC	AGTGGTAAAC	ATGTGGTATT
3	E D E A D Y Y C N S	R D S S G N H V V F				
	730	740	750	760	770	780
1	CGGCGGAGGG	ACCAAGCTGA	CGTCCCTAGG	TGCGGCCGCA	GAACAAAAC	TCATCTCAGA
3	G G G T K L T V L G	A A A E Q K L I S E				
	790	800	810	820	830	840
1	AGAGGatCTG	AatGGGGCGG	CAGGAACTG	TtGAATTTT	TAAGTTAAC	T
3	E D L N G A A	* N C * I F * V N				

Y16 SEQ ID NO: 210



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FIG. 51

Sequence of Y1-Biotag (SEQ ID NO: 211)

1 MEVQLVESGG GVVVRPGGSLR LSCAASGFTF DDYGMSWVRQ
41 APGKGLEWVS GINWNGGSTG YADSVKGRFT ISRDNAKNSL
81 YLQMNSLRAE DTAVYYCARM RAPVIWGQGT LTVTSRGGGG
121 SGGGSGGGG SSELTDPAV SVALGQTVRI TCQGDSLRSY
161 YASWYQQKPG QAPVLVIYGK NNRPSGIPDR FSGSSSGNTA
201 SLTITGAQAE DEADYYCNSR DSSGNNVVFG GGTKLTVLGG
241 GGLNDIFEAQ KIEWHE

FIG. 52

Y1-cys-kak scFv (SEQ ID NO. 212)

1 MEVQLVESGG GVVRPGGSLR LSCAASGFTF DDYGMSWVRQ
APGKGLEWVS GINWNGGSTG 60

61 YADSVKGRFT ISRDNAKNSL YLQMNSLRAE DTA VYYCARM
RAPVIWGQGT LVT VSRGGGG 120

121 SGGGSGGGG SSEL TQDPAV SVALGQTVRI TCQGDSLRSY
YASWYQQKPG QAPVLVIYGK 180

181 NNRPSGIPDR FSGSSSGNTA SLTITGAQAE DEADYYCNSR
DSSGNHVVFG GGTKLTVLGG 240

241 GGCKAK